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THE JOHN ALEXANDER MONOGRAPH SERIES

on Various Phases of Thoracic Surgery

A Memorial to John Alexander (1891-1954)
Professor of Surgery, University of Michigan

THE TREATMENT OF BRONCHIAL NEOPLASMS

By

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and
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with a chapter on
BRONCHIAL ADENOMA
by
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Dedicated with sincere appreciation to Stuart W Harrington, friend, and Cameron Haight, colleague, of John Alexander

Preface

THE INCREASING MAGNITUDE of the problem of bronchial neoplasms particularly cancer of the lung, prompts those who have treated patients having these tumors to evaluate their past experience It is only through such evaluations that future application of treatment using available methods can be improved Increasing experience is beginning to show that slavish adherence to the traditional radical approach to the surgery of cancer may actually be resulting in the shortening of lives of some of the victims of this disease It has now been a quarter of a century since Graham's first successful surgical removal of a total lung for bronchogenic carcinoma The bright promise of this brilliant achievement, both for resectability and satisfactory long term survival has not been realized in the vast majority of patients having this disease The results of surgical treatment make it evident that surgical removal for bronchogenic carcinoma has not measured up to the heavy burdens placed upon it in most instances, and emphasize the need for a re evaluation of the rationale of treatment based on the temporal factor alone

To date it has been impossible to correlate better end results with early treatment solely from the standpoint of time Since surgery has been available for treatment, there has been an intensive campaign both within the medical profession and in the field of lay education to detect malignancies of the lung in a stage when they are still localized to the primary site However, over the years, the operability rate for bronchogenic carcinoma has remained at the same level for all patients as well as being practically the same for those who came early and those who arrived late for treatment It would appear that the temporal factor is of lesser importance than the biologic factors in determining the prognosis of patients with bronchogenic carcinoma

The authors hope in presenting their philosophy of treatment evolved from a combined experience of 1180 patients having bronchogenic carcinoma that they can contribute to an improvement in the results of the surgical and nonsurgical treatment of this disease They feel that this can be done not so much through a contribution to the technique of resection or the management of the patient undergoing surgery, but rather by a better selection of patients for surgical excision, and to an improvement in the quality of survival through application in patients with suitable lesions of selective resections of the lung It is realized that this attitude may represent a departure from the ideal of the traditional radical approach to the surgery of cancer of an internal organ It is believed, however, that the traditional concept must be tempered in the case of bronchogenic carcinoma by practical considerations of function

Because surgical therapy can be applied only to approximately one third of the patients having malignant bronchial neoplasms, many patients become candidates for irradiation or drug therapy These modalities may be effectively used to con

trol distressing symptoms and prolong useful living

The challenge to the surgeon today is to learn more about the biologic characteristics of the various types of bronchial neoplasms so that he will know which lesions are operable, and which are treated better by other means, which will be benefited by radical resections, and which may be treated by more conservative resections without sacrifice of survival time but with the attendant advantages of a better quality of survival

Acknowledgments

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R R S
D L P

Contents

The Treatment of Bronchial Neoplasms

Introduction

THE RAPIDLY RISING incidence of bronchogenic carcinoma presents a challenging problem to the entire medical profession The fact that the rising incidence is a real one and is not due to increased interest in and more accurate diagnosis of this malignancy is accepted almost universally by physicians who have dealt extensively with this disease Doctor Lester Breslow,[1] Chief of the Bureau of Chronic Diseases of the California Department of Public Health, states that there has been an increase of 400 per cent of carcinoma of the lung in males since 1930 The death rate in 1930 from bronchogenic carcinoma was 7 per 100,000 'but by 1954 had reached 28 5 per 100 000" The corresponding figures for females was 2 8 in 1930 and 5 in 1954 During this same period other malignancies occurring in males, principally carcinoma of the stomach had shown a decline This indicates that the increase could only partially be explained by the increasing life expectancy due to better control and treatment of diseases of the earlier periods of life Doctor Breslow predicted that by 1960 carcinoma of the lung would be a major problem It was his opinion that we can normally expect a decline in cancer mortality except for those cancers caused by agents we introduce into our environment such as cigarettes, smog and radiation fallout

The cause of the rising incidence of bronchogenic carcinoma has been extensively investigated This investigation has been in the form of statistical studies and observation of the irritating effects on the bronchial mucosa of various inhaled irritants Statistical studies have pointed consistently to an association between heavy cigarette smoking and carcinoma of the lung (Fig 1) It is also recognized that inhalation of tobacco smoke is only one factor — although probably the most important one Inhaled fumes from the petroleum industry the exhaust of automobiles, coal tar products on roads, gases from the welding process, radioactive gases

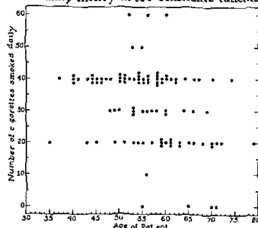


Fig 1

and exposure to certain metals, especially cobalt — all contribute to bronchial irritation that may influence the formation of bronchial neoplasms The suggestion that previous pulmonary infections might be a factor in the formation of bronchial neoplasms has been discarded However, recently there has been renewed interest

the incidence of bronchogenic carcinomas arising in and adjacent to fibrotic areas in the lung (Fig 2)

The careful postmortem studies of Auerbach[4] have shown the changes in the epithelial lining of the bronchi from ciliated columnar to squamous metaplasia and then in local areas on to carcinoma in situ and finally to invasive malignancy His studies show that these changes occur consistently more often in men who have smoked cigarettes excessively as compared to men who have been either light or nonsmokers In individuals who have died from bronchogenic carcinomas there were a significantly greater number of areas of carcinoma in situ than in other individuals dying of unrelated causes This observation explains the rare occurence of a second primary bronchogenic carcinoma in an individual who has previously received an apparent cure following surgical resection of a previously detected cancer of the lung (Fig 3)

The observation that there is an association between heavy cigarette smoking and cancer of the lung unfortunately is not helpful in curbing the rising incidence of this disease It is a human failing that where pleasure is involved consequences are not heeded James Ewing the noted pathologist, over thirty years ago pointed out the relationship between smoking and cancer of the lung He said that he did not believe dissemination of this knowledge would change smoking habits but that he did think the public had the right to be informed The authors are in agreement with this attitude

The advent of surgical therapy was the first ray of hope offered the victims of this





Fig 2a The lesion indistinctly seen in the film of the chest of a 44 year old man was the source of small hemoptyses

Fig 2b Planography more distinctly outlines the nodule which has developed in a region which is the site of bullous emphysema This combination is highly suggestive of a bronchial neoplasm arising in scar tissue The lesion was resected by lobectomy The prognosis for cure is good because disturbance of lymphatics and vascular supply by the bullous emphysema limits the opportunity of the neoplasm to metastasize

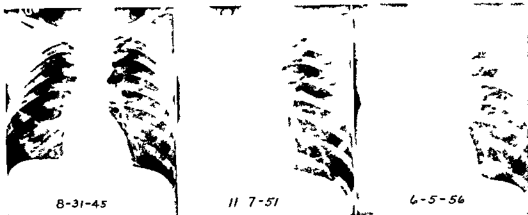


Fig 3 Eleven years following right pneumonectomy for bronchogenic carcinoma this patient developed a secondary primary bronchogenic carcinoma in the left lung which caused his death

disease Before surgical therapy became feasible there was little incentive to the physician to diagnose bronchial neoplasms while still in a localized stage since no treatment was available The burden was now placed on the medical profession to differentiate cancer of the lung from other pulmonary diseases and make surgical treatment available to the patient In the first wave of enthusiasm many patients had their chests explored and lungs resected who now would be considered not suitable for surgery It took time and experience to determine the limitations of surgery in coping with this disease

The authors are reporting their experience with 1215 patients diagnosed as having bronchial neoplasms treated during the period from September 1945 to December 1957 One thousand one hundred eighty of these tumors were bronchogenic carcinomas and 35 were adenomas of the bronchi All of these patients were seen in private practice and were cared for personally by the authors Not included are a number of patients diagnosed as having cancer of the lung treated by the staff in a city county hospital with which the authors are associated in the capacity of consultants Many patients included in the series were found to be unsuitable candidates for surgical therapy because of evidence of extension of the neoplasm beyond the involved lung Some of these were seen by the authors on only one occasion These patients are included in the total series however in order to present as far as possible an unselected group The inclusion of these patients broadens the base of observation but lowers the percentages of operability resectability and total salvage A few of these patients had only a clinical diagnosis without tissue confirmation The course of the disease over a period of time served to confirm the diagnosis Cases where the subsequent course was not known or did not conform to the expected pattern of progression were excluded from the series

The attitude of the authors during the twelve year experience being reported has not remained static In our early experience we accepted the temporal theory of the evolution of a neoplasm We were impressed also by the prevailing opinion that total pneumonectomy was the operation of choice in the surgical removal of a cancer of the lung Even during this early period however encouraged by reports of Churchill and others we removed small peripheral neoplasms by selective resection Our early enthusiasm stimulated by a misguided urge to help the patient out of his difficulty '

to a high percentage of exploratory thoracotomies During this period there was also a tendency to try to resect the neoplasm once the chest was opened even though it was obvious that the lesion could not be completely resected It did not take long to find that this overaggressive application of surgical therapy was not increasing survival time of patients to whom it was applied Gradually, greater care was used in selection of patients for surgery Impressed by the observation that patients with selective resections were experiencing just as long and a better quality of survival lobectomy became the operation of choice (Fig 4) Conservation of pulmonary tissue was practiced even to the extent of utilizing bronchoplastic procedures Since 1950 our rationale of treatment as far as the application of surgery is concerned has changed very little Realizing the limitations of surgery we are presently employing both irradiation and chemotherapy to a greater extent

It has now been a quarter of a century since Graham performed the first successful pneumonectomy for bronchogenic carcinoma in 1933 The bright promise of this brilliant achievement both for resectability and satisfactory long term survival has not been realized in the majority of patien[ts] having this disease In the authors' seri[es] of 1180 patients, half of the patients ha[d] lesions which were inoperable when fir[st] seen, and another 15 per cent were foun[d] to be nonresectable at the time explorator[y] thoracotomy was done (Fig 5) One thir[d] of the patients had resectable lesions, and [in] only a small percentage of these were the[ir] carcinomas sufficiently well localized to per[mit] long term survival The increasin[g] frequency of bronchogenic carcinoma an[d] the results of surgical treatment which mak[e] it evident that surgical removal for th[is] lesion has not measured up to the heav[y] burdens placed upon it emphasize the nee[d] for a re evaluation of the rationale of treat ment

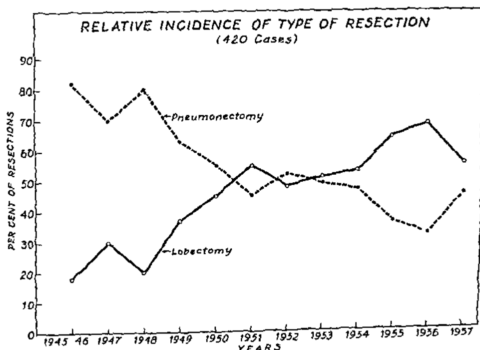


Fig 4 Relative incidence of the type of resection for bronchogenic carcinoma plotted by years 1945-46 through 1957

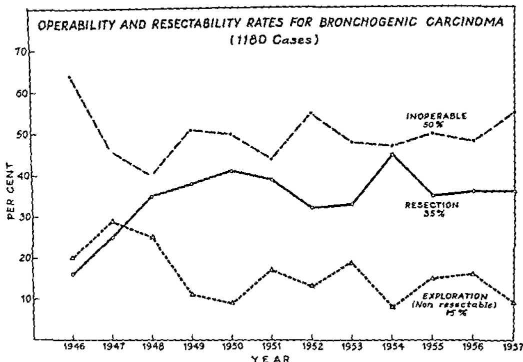


Fig 5 Operability and resectability rates for 1180 cases of bronchogenic carcinoma seen 1946–1957 The operability rate of 50 per cent and the resectability rate of about 35 per cent remain remarkably stationary

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The Rationale of Treatment

THE RATIONALE OF THERAPY for bronchogenic neoplasms is necessarily intertwined with the general knowledge of cancer in any location Two antithetic theories exist at the present time to explain the spread of cancer and its prognosis The first of these, the *classical temporal theory* emphasizes the function of time and states that a cancer begins as a localized disease, grows in a steady and irrevocable manner, spreads to the regional lymph nodes in time, and with the passage of more time disseminates throughout the body The second and more modern theory of *biologic predeterminism* states that the behavior of a neoplasm in an individual host is an expression of a biologic potential established in its inductive phase Its characteristics are established in the preclinical phase and remain more or less constant throughout its life, although it may undergo *intermittent periods* of growth and quiescence Cognizance of the respective merits of each theory forms the foundation for the rationale of treatment of bronchogenic carcinoma

Classical Temporal Theory

The classical temporal theory has been generally accepted by surgeons and forms the logical basis for the traditional radical approach to carcinoma It has been widely promulgated, both within the profession and to the lay public, that the prognosis in cancer can be altered by early and wide excision of the neoplasm together with the regional lymph bearing area This has occurred in spite of evidence to the contrary that it is often impossible to correlate better end results with early treatment from the standpoint of time alone *In this concept* the existing methods of diagnosis and treatment of cancer are considered adequate and responsibility for any delay in detection is placed alike on the physician and the individual concerned The surgeon is often absolved of the consequences of failures of therapy on the basis that the patient arrived too late to obtain a good result This is generally accepted in spite of the opposing evidence that some of the long term survivors are those with the longest histories of their disease who arrived late for treatment

Husfeldt[1] has found in Denmark that the operability rate for bronchogenic carcinoma is practically the same for those who come *in early and* those who arrive late for treatment He explains this apparent paradox to the doctrine of the temporal theory on the basis that the more rapidly growing carcinomas produce progressive symptoms in a shorter period of time but are frequently inoperable On the other hand the more slowly growing tumors are accompanied by less pronounced symptoms but may still be operable when the patient finally presents himself for treatment

Because it is reasonable to assume on the basis of circumstantial evidence that early detection and treatment may prolong survival time in some individual patients, it is often disregarded that to diagnose a can

cer earlier is to increase survival time by a similar period even without treatment (Fig 1) Rigler[*] has shown in a retrospective study of roentgenograms of the chests of patients with bronchogenic carcinoma that in over half of the hundred patients followed by this means their lesions were found to antedate either symptoms or diagnosis by two years or more and as long as fourteen years The average survival time after institution of therapy was only nine months whereas before this they had lived with their cancers for years Earlier diagnosis would have resulted in a proportionately longer survival time after the diagnosis was made regardless of treatment

Biologic Predeterminism

The theory of biologic predeterminism ennunciated by Ian MacDonald[*] and supported by Crile[*] is a tenable concept which explains the course and prognosis of cancer on the basis of the biologic characteristics involved The cell type location and the resistance of the host largely determine the pattern of behavior and prognosis and the factor of time becomes less important as a consequence only of the biologic traits of the particular neoplasm involved

Application of the theory of biologic predeterminism to bronchogenic carcinoma explains the variegated pattern of behavior and prognosis in this neoplasm and places the rationale of treatment on a logical basis The authors found in 1951[11] as a result of a study of 362 patients with bronchogenic carcinoma that in 25 per cent the initial complaint which prompted the patient to seek medical advice was one indicating inoperability such as headache due to cere

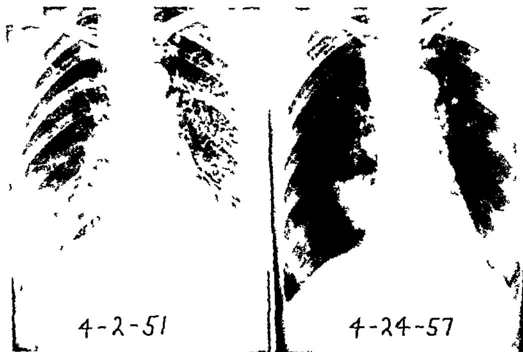


Fig 1 Roentgenograms of the chest six years apart of a woman found to have proven inoperable carcinoma of the middle lobe with mediastinal node involvement in 1957 The patient has seven years without treatment Earlier diagnosis v ... resulted in survival for a si ... regardless of

bral metastases, loss of voice due to involvement of the recurrent laryngeal nerve, pain due to involvement of the brachial plexus, venous distention due to involvement of the mediastinum, painless pleural effusion, dysphagia due to involvement of the esophagus, involvement of such distant organs as bone and peritoneum, or subcutaneous metastases due to generalized dissemination of cancer. The occult nature of the primary lesion, the insidious onset, the paucity of symptoms, and the rapid growth with early progression to metastasis in this group make the diagnosis and treatment impossible to attain during an early localized stage. About 20 per cent of patients have an undifferentiated carcinoma, widely recognized for its rapid dissemination and considered by many as a sign of inoperability in itself. If the 25 per cent of patients in whom the initial complaint indicated inoperability are added to the 20 per cent who have an undifferentiated carcinoma and allowance is made for overlapping of the two groups, we estimate that roughly 35 per cent of the patients having bronchogenic carcinoma will have the type of tumor and lack of resistance to predetermine inoperability biologically. The function of time is not important in this group. In contrast, low grade epidermoid carcinomas may remain well localized for long periods of time, produce less pronounced symptoms over several years, and yield long periods of survival after resection is finally done. These lesions are late in point of view of time but favorable from the standpoint of biologic characteristics and localization. Many of the patients who survive for long terms following resection are in this group with histories extending over several years.

A cancer may be early biologically but late chronologically. The observation that a particular lesion, such as a pulmonary nodule, is symptomless may give the impression that it is an early lesion in point of time but this may or may not be true (Fig. 2). The fact that it may remain localized and symptomless for a long period of time, in some cases for years, is a direct expression of its biologic character. The amount of time required for its eventual growth peripherally or centrally to produce symptoms depends on its cell type, the resistance of the host, and its original location. Time is but a consequence of these factors. The term *early* applies more to the degree of localization rather than to its temporal aspects. The phrase "detection in an early phase" becomes preferable to "early detection" with its chronologic connotation.

The resistance of the host, the third factor of importance in the theory of biologic predeterminism, can be illustrated on the basis of circumstantial clinical evidence. Recent reports in the literature attest to spontaneous cures of cancer. Evidence is also available that malignant neoplasms may undergo alternating periods of growth and quiescence if not actual regression. Recurrence from metastases after many years of quiescence without clinical evidence of disease is not uncommon. Some individuals treated for cancer have attained unexpected and unpredictable long periods of survival (Figs. 3 and 4). These vagaries in the natural history of cancer infer a degree of natural resistance on the part of the host. A sharper appreciation of this biologic factor may enable a more logical utilization of various surgical, radiotherapeutic or chemotherapeutic techniques to influence retardation of tumor growth with prolongation of useful and comfortable living.

Evidence of tissue resistance to the spread of cancer cells is found in the lymphatic system. Lymphocytic and round cell infiltration found in experimental studies of tumor transplants led Ewing to conclude that "the lymphocyte is an important agent of defense against tumor growth." The rarity of metastatic lesions in the spleen in contrast to the liver suggests that cells

find it an unfavorable organ for growth Black and Speer[1] as a result of investigating the relationship between the survival of cancer patients and various structural features of their primary cancers and regional lymph nodes found a direct relationship between the degree of sinus histiocytosis and prolonged survival in breast and gastric carcinomas The favorable prognostic significance of sinus histiocytosis was found to be independent of the presence or absence or the amount of re



Fig 2 Bronchogenic carcinoma removed by lobectomy May 1949 after hemoptysis occurred Previous roentgenogram of the chest in November 1945 revealed a nodule in the left third interspace This cancer was early biologically but late chronologically The patient has survived ten years after lobectomy and over twelve years after the earliest evidence of the lesion demonstrating its favorable biologic character

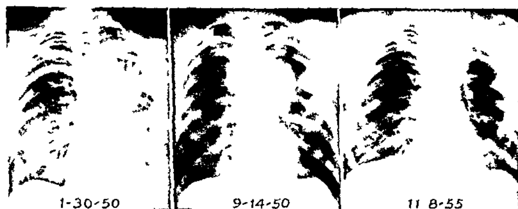


Fig 3 Roentgenograms of the chest of a patient who has survived over eight years following an exploratory thoracotomy in January 1950 which proved the lesion to be a nonresectable small undifferentiated bronchogenic carcinoma Irradiation therapy was given in September 1950

gional node metastases the grade of the original tumor or the completeness of surgical eradication of the disease Since sinus histiocytosis is an uncommon finding in the lymph nodes of cancer free humans and since it is a reactive change in the tissue of a cancerous host associated with increased survival it is believed to be an expression of host resistance

The possible role of the lymph nodes in preventing spread of cancer has received little consideration by surgeons In general the lymph nodes are considered as passive receptors of the actively growing neoplasm and wide dissection with removal in conjunction with radical excision of the primary neoplasm is regarded as essential for adequate cancer surgery However the conclusions of McWhirter and Haagensen and Stout suggest that there is a group of breast cancers in which harm is done by resecting the involved lymph nodes and that by not dissecting the axilla the risk of dissemination of malignant cells to distant sites is reduced The authors are likewise impressed by the fact that in some patients having an extensive undifferentiated bronchogenic carcinoma the appearance of distant metastases may have been hastened by radical resection The explosive spread of certain cancers after a period of slow progression or even quiescence infers some breakdown in the resistance of the host This may be induced by unwise surgical procedures with dissemination of the cancer cells into blood vessels and lymphatics through interference with the protective lymph barriers

Carcinoma In Situ

Carcinoma *in situ* has been found often in association with an epidermoid carcinoma of the bronchus on the ipsolateral or contralateral side Ryan and McDonald reported the study of necropsy specimens of the opposite or remaining lung after pneumonectomy for a squamous cell carcinoma on the primary side They found *in situ*



Fig 4 Roentgenograms of the chest of a patient who survived seven years following irradiation therapy for a proven nonresectable epidermoid carcinoma Death was due to cerebral arteriosclerosis

lesions of the squamous cell variety in five of 39 cases studied death having occurred from a few days to three years after the pneumonectomy Auerbach[1] has found in *situ* carcinoma in the bronchial tree bilaterally in a high percentage of autopsy specimens studied The occurrence of *in situ* carcinoma bilaterally with or without an associated carcinoma of the bronchus illustrates the futility of one sided complete bronchial excision in an attempt to eradicate all precancerous lesions Just as *in situ* lesions of the cervix uteri have a long latent period and may never become invasive in many patients so may *in situ* lesions of the bronchus Since these lesions are multicentric and undoubtedly have a long latent period, radical removal of all sites of involvement becomes both impossible and unnecessary

Long term survivors may run the risk of a second carcinoma developing from one of these *in situ* lesions The authors have seen three such cases the second carcinoma developing in the contralateral lung nineteen months five years and eleven years respectively after resection of the first squamous cell carcinoma (Figs 5 and 6) In one of these cases the second lesion was resected by means of a segmental resection nineteen months after a lobectomy for the first carcinoma on the contralateral side The possibility of the later development of a second carcinoma from an *in situ* lesion favors the use of an adequate lobectomy where possible for the first lesion

Carcinoma *in situ* presents a challenge for early diagnosis Cytologic study of bronchial secretions may lead to the detection of some of these lesions prior to or shortly after their development into an invasive carcinoma It is in this regard that detection of bronchogenic carcinoma in an early phase may find its true application The following case reports illustrate the accomplishment of this ideal

Case 1 L L H, a 59 year old man with symptoms of a pneumonitis of the right lung of one week s duration Plain roentgenograms revealed an obstructive pneumonitis in the anterior segment of the right upper lobe (Fig 7) Examination of bronchial secretions and sputum revealed atypical cells suspicious of malignancy (Papanicolaou Class IV) A right upper lobectomy was done for an epidermoid carcinoma 4 mm in size in the anterior segmental brochus of the right upper lobe (Fig 8) Sections through the neoplasm and bronchus re



Fig 5 Roentgenograms of the chest of a patient in August 31 1945 prior to a right pneumonectomy for an epidermoid carcinoma November 7 1951 six years later and June 5 1956 fourteen years after the onset of symptoms due to the carcinoma in the right lung and 11 years after pneumonectomy illustrating a second separate primary epidermoid carcinoma of the

2 2 56

9 20 57

Fig 6 Roentgenograms of the chest of a patient illustrating separate primary epidermoid carcinomas first in the right lung in February 1956 resected by lobectomy and nineteen months later a lesion in the left lung removed by a segmental resection

Fig 7 Roentgenograms of the chest revealing an obstructive pneumonitis in the anterior segment of the right upper lobe





Fig 8 (Upper) Photograph of the surgical specimen Case 1 following a right upper lobectomy showing a small intralum nal carcinoma 4 mm in size in the orif ce of the anterior segmental bronchus

Fig 9 (Lower) Photomicrograph of the carcinoma Case 1 revealing epithelial metaplasia carcinoma *in situ* and invasive carcinoma





Fig 11 (Upper) Photograph of the surg cal specimen Case ? showing the intralum nal carcinoma in the orifice of the anter or segmental bronchus of the left upper lobe

Fig 12 (Lower) Photom crograph of the carcinoma Case 2 reveal ng ep thel al metaplast c changes and early invasive carcinoma

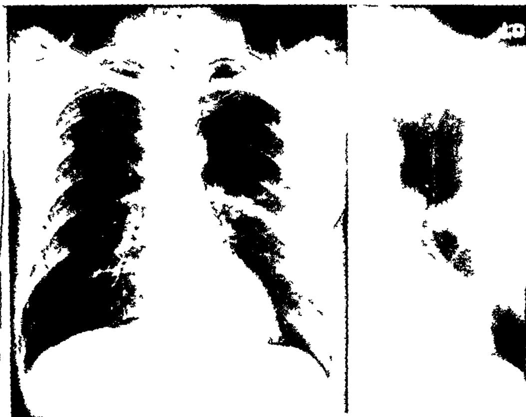


Fig 10 Case w Plain roentgenogram and plan gram of the chest revealing a small hilar carcinoma in the anterior segmental bronchus of the left upper lobe producing hemoptysis

vealed epithelial metaplasia carcinoma in situ and early invasive carcinoma (Fig 9)

Case 2 M S a 50 year old man had hemoptysis of ten days duration Plain roentgenograms and planigrams revealed a nodular density in the anterior segment of the left upper lobe (Fig 10) Bronchial secretions were positive for malignant cells Left upper lobectomy was done for an early epidermoid carcinoma 5 mm in size in the anterior segmental bronchus of the left upper lobe (Fig 11) Sections through the carcinoma and bronchus re vealed normal mucosa carcinoma in situ and early invasive carcinoma (Fig 12)

Operative Approach

Application of the ideal of the traditional radical approach to the surgery of cancer must be tempered in the case of broncho genic carcinoma by practical considerations of function Because bronchogenic carci nomas frequently occur in association with pulmonary emphysema and reduced func tion preservation of lung tissue is of the utmost importance Survival rates alone are not the only measure of therapeutic effec tiveness The differences in mortality be tween radical and conservative approaches and the quality of survival are equally im portant gauges of therapeutic efficiency There is a great difference between the pa tient who survives but is disabled and the one who lives for a similar period of time but is able to continue with normal or near normal activity comfortably Furtherm

the advantages thought to be gained in increasing life expectancy by the radical approach to bronchogenic carcinoma may be partially or completely offset by its injurious character

Operability and *resectability* are not synonymous terms A neoplasm may be considered operable but be found to be nonresectable when an exploratory thoracotomy has been done Similarly, a particular lesion may be *resectable* by virtue of its size and location but be inoperable because of cell type, metastasis either distant or local, or poor cardiac and pulmonary function Exploratory thoracotomy for a nonresectable carcinoma is to be avoided where possible since it carries a definite risk of surgical mortality without benefit to the patient except the confirmation that no surgical treatment is feasible Similarly, the tendency to increase the scope of the operation or to perform palliative resections knowingly leaving behind carcinoma is likewise undesirable because of the attendant high mortality and lack of benefit to survival time

The ability to resect a particular bronchogenic carcinoma should not be the sole determining factor in the surgeon's consideration but rather what benefits are reasonable to expect on the one hand weighed against the possible harm that may accrue on the debit side from resection The challenge is to learn enough about the biologic characteristics of the various types of bronchogenic carcinoma so that it will be known which lesions are suitable for surgery, which will be benefited by radical resections, which may be treated by more conservative resections with a better quality of survival, and which types will be harmed by resection through interference with the lymph node barrier and dissemination of cancer cells through the lymphatics and blood stream In some cases a period of quiescence may be induced by irradiation or chemotherapy Pre-operative irradiation therapy to block the lymphatics as well as to induce a period of slower growth as suggested by Dunphy[3] may require further evaluation

Irradiation and Chemotherapy

Since surgical resection is possible in only one third of the patients having bronchogenic carcinoma, other modalities of treatment such as irradiation and chemotherapy are applicable to the remaining patients. These therapeutic methods are subject to the same disadvantages as is surgery in that the lesions chosen for therapy frequently are biologically unfavorable or disseminated Nevertheless, judicious application of irradiation or chemotherapy singly or combined may induce quiescence in growth relief of distressing symptoms, and in a few patients prolongation of life

The combination of irradiation therapy or chemotherapeutic agents with surgical resection in the treatment of bronchogenic carcinoma warrants further exploration By means of various combinations of therapy some patients may become suitable candidates for more definitive procedures

SUMMARY

Whereas early detection and treatment may prolong survival time in some patients, the temporal factor is of secondary importance to the biologic factors in the rationale of treatment of bronchogenic carcinoma Application of the theory of biologic predeterminism to bronchogenic carcinoma explains the variegated pattern of behavior and prognosis in this neoplasm and places the rationale for treatment on a logical basis The cell type location, and the resistance of the host largely determine the pattern of behavior and prognosis The factor of time becomes less important as a consequence only of the biologic traits of the particular neoplasm involved A carcinoma may be early biologically but late chronologically The term *early* applies more to the degree of localization rather

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Application of the traditional radical ap ›roach to the surgery of cancer must be ɛmpered in the case of bronchogenic carci oma by practical considerations of the vital ınctions of the lung and the biologic fac rs involved The differences in mortality tween radical and conservative ap ›aches and the quality of survival are im 'tant gauges of therapeutic efficiency The biologic characteristics of a particu neoplasm determine suitability for surgi cal resection on the basis of localization The challenge is to learn enough about the biologic characteristics of the various types of bronchogenic carcinoma so that it will be known which lesions are suitable for surgery, which will be benefited by radical resections which may be treated by more conservative resections with a better quality of survival and which types will be harmed by injudicious application of surgical tech niques being better treated by means of irradiation or chemotherapeutic methods

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Selection of Patients for Surgery

BECAUSE OF THE BIOLOGIC characteristics of bronchogenic carcinoma, any improvement in survival rates following resection can be achieved mainly through a better selection of the biologically early lesions for surgical therapy The fact that certain patients may have localized lesions that can be cured by surgical excision does not mean that surgical therapy will be applicable to all patients having bronchogenic carcinoma It is not prudent to submit a patient to a surgical procedure which is destined to prove fruitless and perhaps harmful Even an exploratory thoracotomy for a nonresectable lesion is attended by a significant mortality, will inevitably add to morbidity, and will very likely reduce the period of survival

It is the responsibility of the surgeon to appraise carefully the patient who has a bronchogenic carcinoma from the standpoint of biologic characteristics and for any evidence of extension of the disease beyond the limits of possible surgical excision before reaching the decision that surgery is advisable Other factors not directly connected with the disease being treated (age, general physical condition, pulmonary and cardiac function, and other diseases carrying a grave prognosis) should be carefully evaluated to determine the ability of the patient to tolerate the proposed surgery, and whether or not as a result of the surgery the patient's prospect of survival in comfort can be improved In weighing these factors other methods of treatment carrying less risk, such as irradiation therapy and chemotherapy, must be kept in mind These other modalities of treatment may allow longer prolongation of life in comfort for patients having a localized lesion in whom other considerations make surgical excision inadvisable, if the carcinoma is biologically unfavorable, or if it has extended beyond the limits of surgical excision

BIOLOGIC FACTORS

Owing to the biologic characteristics of bronchogenic carcinoma half of the patients have lesions which are inoperable when first seen and another 15 per cent are found to be nonresectable at the time of exploratory thoractomy One third of the patients have resectable lesions and in only a small percentage of these are the carcinomas favorable for long term survival The biologic factors of cell type location and resistance of the host largely determine the pattern of behavior and prognosis Appreciation of the importance of this concept will lead to a better selection of patients for surgery and improved survival rates

From the standpoint of evaluation of the individual patient having a bronchogenic carcinoma the cell type the location the rate of progression of the lesion, and the length of history of symptoms are all important considerations Twenty percent of the patients have a small cell undifferentiated carcinoma widely recognized for its rapid dissemination and considered by many as a sign of inoperability in itself Frequently patients with carcinomas of this type manifest signs of rapid progression such as

roentgenographic evidence or early deterioration and have a paucity of symptoms or a short history They may present themselves because of symptoms due to a metastasis In contrast the patient having a biologically favorable low grade epidermoid carcinoma frequently has a longer history of specific symptoms definitely localized to the lung and evinces slow progression of the lesion Dependable biopsies of the neoplasm obtained by bronchoscopic examination may well be decisive in arriving at a wise decision regarding the advisability of surgery

Location of the shadow on the roentgenogram as nodular hilar or extremely peripheral is also an important consideration in the evaluation of the individual patient Bronchogenic carcinoma presenting as a pulmonary nodule is resectable in a high percentage of cases and yields high survival rates particularly in the absence of symptoms even though there may be evidence that it has been present a long time In contrast the hilar lesion particularly in the left lung may be disappointing due to extension along the hilum to the mediastinum not readily visualized within the arch of the aorta Laminography is often of assistance in evaluating possible mediastinal extension or metastases Extreme peripheral lesions even though they involve chest wall may be resectable

ABSOLUTE SIGNS OF INOPERABILITY

There are certain evidences of extension of a bronchogenic carcinoma that should be recognized as absolute signs of inoperability in contrast to those that are only suggestive

Distant Metastases

The presence of distant metastases as a general rule makes surgical excision of the primary lesion inadvisable

Cerebral Metastases Brain tumors due to blood borne metastases are common in bronchogenic carcinoma Neurosurgeons are so well aware of this fact that in patients presenting symptoms of a brain tumor routine x rays of the chest are made in order to rule out the presence of a primary bronchogenic carcinoma (Figs 1a and 1b) Although it may be true that in approximately one third of patients having a metastasis to the brain from a bronchogenic carcinoma the metastasis will be a single one combined attacks upon the cerebral metastasis and the primary lesion by surgery have not been rewarded by a significant increase in survival time Any palliation that has been afforded has usually been due to the removal of the cerebral lesion and not due to pulmonary resection removing the primary tumor Irradiation therapy over the cerebral lesion may provide some palliation of symptoms with less risk of causing additional neurologic defects or operative mortality

Spinal Metastases The spine is also a common site for blood borne metastases from bronchogenic carcinomas The occurrence of a localized lancinating pain usually in the low thoracic or high lumbar region radiating along known nerve pathways is the usual symptom caused by such metastases The severe unrelenting character of the pain will usually differentiate it from the pain caused by a prolapsed disc There is usually little roentgenographic evidence of the metastases as shown by erosion of the vertebrae The intervertebral disc may be involved The occurrence of a pain of this type in a patient known to have a primary bronchogenic carcinoma and especially if it is of short duration is sufficient to contraindicate pulmonary resection Although palliation can be effected by irradiation therapy over spinal metastases the period of improvement is usually quite short The pain as a rule recurs and often complete paraplegia will occur before death

Abdominal Metastases. Metastases to the abdominal organs chiefly the liver and adrenals and occasionally the kidneys a

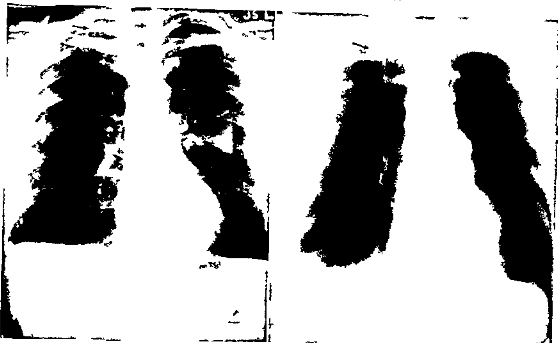


Fig 1a This roentgenogram of the chest of a 45 year old man was taken as a *routine study because* of symptoms suggestive of a brain tumor

Fig 1b Stratograph of the chest which gives better delineation of the pulmonary nodule presumed to be a primary bronchogenic carcinoma Before advising that this asymptomatic nodule be resected it should first be established whether or not the brain tumor is a metastatic lesion

peritoneum often occur but may be difficult to detect clinically Involvement of the retroperitoneal nodes also is common in disseminated carcinoma At the time of post mortem examination it is often amazing how much neoplasm is discovered in a patient who exhibits no more than mild lassitude The ability to palpate an enlarged nodular liver in the absence of other forms of hepatic disease is highly suggestive of metastases to the liver and should be considered a sign of inoperability Bronzing of the skin and lassitude out of proportion to obvious disease should make one suspect adrenal metastases An exploratory laparotomy is seldom advisable to establish the presence of metastases within *abdominal* organs Radiographic techniques are of little help in determining the presence of abdominal metastases except in the rare situation where there may be large retroperitoneal masses The incidence of abdominal *nal metastases and the difficulty in diagnos*ing them is one factor in the disappointing short survival of many patients following pulmonary resection for bronchogenic carcinoma

Metastases to Bones Bronchogenic carcinomas commonly metastasize to bones These metastases are usually to the flat bones such as the ribs and skull but oc*casionally they involve the long bones* Metastases to ribs on the involved side or contralateral side may occur Their presence may be detected because of a pathologic fracture that might be confused with a cough fracture Metastatic lesions to bones from malignancies of the lung are of *an osteolytic* type It may be necessary to perform a biopsy of the bone tumor to establish its true nature before deciding that the presence of the bony lesion contraindicates resection of the tumor in the lung

Pulmonary Metastases. Involvement of

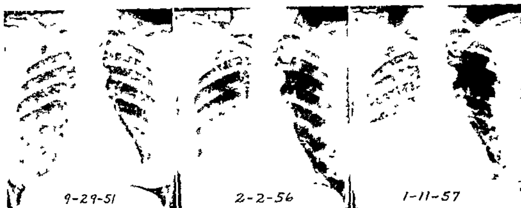


Fig 2a b, c This bronchiolar carcinoma arising in the right lower lobe remained a localized lesion for several years When dissemination occurred the left lung became involved rendering the patient inoperable This case illustrates the importance of advising resection for pulmonary nodules of unknown etiology

the contralateral lung in bronchogenic carcinoma is common as a late development in the type of malignancy being designated as alveolar or bronchiolar carcinoma Metastases may occur rarely in other types of bronchogenic carcinoma Extension through the subcorynal nodes to involve the opposite bronchus occurs occasionally Contralateral pulmonary metastases represent an absolute sign of inoperability (Fig 2a, b, c)

Evidences of Dissemination General dissemination of a bronchogenic carcinoma may be obvious by the occurrence of metastatic nodules in the skin and scalp In the course of a physical examination of a patient the scalp should be carefully palpated for any evidence of nodules that might have recently occurred and escaped detection by the patient If there is doubt as to the nature of the nodule, biopsy should be carried out to establish whether or not a metastasis is present It is obvious that any such sign of generalization of the disease contraindicates pulmonary resection for the primary lesion

LYMPHATIC EXTENSION

The spread of a bronchogenic carcinoma in the lymphatic system becomes complex as soon as it goes beyond the peribronchial nodes On the left side, the spread from the neoplasm in the upper lobe will follow the nodes under the arch of the aorta and then along the paratracheal nodes to reach the supraclavicular nodes in the fat pad overlying the anterior scalene muscle A carcinoma in the left lower lobe may spread along one or both of two lymphatic routes The first would be to the nodes below the inferior vein which communicate with the nodes in the abdomen in the retroperitoneal space The second route would go to the nodes in the corynal region and thence would follow the paratracheal nodes on either side to reach the supraclavicular nodes on either or both sides of the neck

Carcinomas in the upper and middle lobes on the right metastasize along the nodes between the trachea and the vena cava to reach the right supraclavicular nodes in the scalene fat pad Following involvement of the node immediately above the azygos vein the extension may be toward the left to the nodes lying just above the arch of the aorta from which group they could extend upward along the left side of the trachea following the same path as extension from the left upper lobe Neoplasms in the r lower and middle lobe typically m

to the corynal mass of nodes from which they can follow a lymphatic path on either side of the trachea The complex lymphatic system of the chest (Fig 3) affording ample opportunity for spread of the carcinoma along many diverse routes, explains why radical resection of the lungs with an attempt to excise involved lymphatics has been so unrewarding in the treatment of bronchogenic carcinoma

From the foregoing paragraphs it becomes obvious that the presence of lymph nodes in the supraclavicular fossa known to be involved by neoplasm represents a sign of incurability Palpable nodes should be removed for pathologic study to establish this fact When one is presented with a patient having bronchogenic carcinoma in whom bronchoscopic examination might be diagnostic, but there are also palpabl-

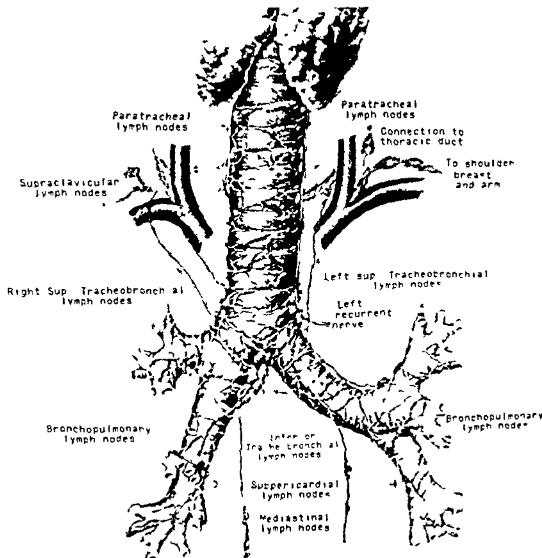


Fig 3 This drawing shows the complex inter communicating lymphatic channels draining the tracheobronchial tree Tumor cells *may* spread early to *the hilar* and to the contralateral lymph nodes through the rather liberal crossed lymphatic *drainage* of the bronchi particularly *through* the subcorynal *region* from the left side

nodes in the supraclavicular fossa, examination of the involved lymph nodes should be carried out first. If these nodes are involved by neoplasm, both the diagnosis and the evidence of incurability have been established and it is unnecessary to subject the patient to the additional procedure of bronchoscopy.

SCALENE NODE BIOPSY

Routine scalene node biopsies have been practiced in some clinics. Cuykendall[1] reports finding metastases to prescalene lymph nodes in 20 per cent of cases in which this examination was done in the absence of palpable nodes. Because of the complex lymphatic system of the chest, if this practice is to be followed, bilateral scalene node biopsies would have to be done. It is doubtful whether it is advisable to subject every patient suspected of having a bronchogenic carcinoma to scalene node biopsies. When the physician senses, however, that the patient being considered represents a poor candidate for excisional surgery, or there is roentgenological evidence of mediastinal node involvement (Fig. 4), examination of the nodes in the scalene fat pad, even though

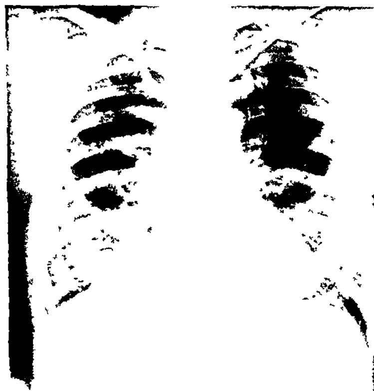


Fig. 4. The widening of the mediastinum on the right is sufficient evidence of nonresectability in the case of this 64 year old man. Even though bronchoscopy and cervical node biopsy did not result in pathologic confirmation of bronchogenic carcinoma, exploration of the chest was not advised. Exploratory thoracotomy in this type of case is of little value to the patient and may result in loss of survival time. Irradiation therapy was advised. A cerebral metastasis became evident within one month of the taking of this film.

is not accompanied by fever Examination of fluid aspirated from the chest in such a case will usually reveal neoplastic cells The fluid may or may not be bloody in appearance but usually red blood cells will be numerous when examined microscopically Surgical resection is inadvisable in the presence of fluid positive for carcinoma cells Pleurectomy has been advised as a palliative procedure in order better to control the pleural effusion The availability of radioisotopes and nitrogen mustard the use of which seems to accomplish approximately the same result now makes pleurectomy a less useful operation

Pleural effusion may also be present as an indication of complete obstruction of a major pulmonary vein due to a tumor thrombus or occlusion of the vein by infiltration of the tumor around it In addition to the pleural effusion the lobe or lung beyond the obstructed veins will be edematous causing it to cast a solid shadow in the roentgen film of the chest without evidence



Fig 5 The complete opacity of the right hemithorax suggests a massive

pulmonary veins by the neoplasm indicates inoperability

of a concomitant loss of volume (Fig 5) The pleural fluid will be high in fibrin content and there may be fibrinous deposits of the chicken fat clot type within the pleural cavity Aspiration of the pleural cavity in this situation will yield a much smaller quantity of fluid than one expects to get as judged by the physical findings and the roentgen appearance of the chest Neoplastic cells usually cannot be recovered from fluid secondary to venous occlusion The occurrence of fluid in the presence of an engorged lobe or lung is a sign of inoperability

Pleural fluid may also accompany atelectasis secondary to bronchial obstruction by neoplasm in a major bronchus When there is bronchoscopic or bronchographic evidence of an obstruction of a major bronchus and evidence of suppuration beyond the blocked bronchus as shown by fever and toxicity the presence of fluid *does not* represent a contraindication to resection Typically neoplastic cells are not found in fluid occurring secondary to atelectasis and suppuration of the lung distal to a bronchial neoplasm

In summary the question of whether or not the presence of pleural fluid complicating a bronchogenic carcinoma indicates a sign of inoperability depends upon the detection of neoplastic cells in the fluid and the determination of whether or not the fluid is secondary to occlusion of a major pulmonary vein

BRACHIAL PLEXUS INVOLVEMENT

Gross invasion of the brachial plexus accompanied by swelling in the supraclavicular fossa Horner s syndrome and radiologic evidence of osteolytic destruction of the posterior portion of the upper ribs close to the spine presents an impossible technical problem to one attempting to eradicate such a lesion Invasion by a peripheral bronchogenic carcinoma causing pain along the ulnar distribution to the hand and the bracheocutaneous nerve to the inner surfac of the arm does not preclude a successfu en bloc resection of the involved lobe o the lung with a *portion of the chest wall* We are at present testing the combinatio of irradiation therapy followed in six t eight weeks by *resection in this type o* lesion (Fig 6a and b) The morbidity i so severe and so often prolonged in th case of the *superior sulcus tumor that pal*nation of pain alone is justifiable even i the face of causing neurologic defects i *the hand and arm on the involved side*

BRONCHOSCOPIC OBSERVATIONS

Observations made at the time of bron choscopy *may reveal evidence of extensio* of the neoplasm sufficient to rule out th possibility of a successful resection Th presence of visible neoplastic tissue at th level of the *carina or trachea representin* a direct extension from neoplasm originat ing in a bronchus is a sign of inoperability If the visible neoplastic tissue can be see *within 2 cm of the carina* a carin biopsy should be done even though th mucosa at this point appears normal sinc neoplastic cells may be demonstrated in th submucosal plane or in the lymphatic *Gross fixation* of a major bronchus wit gross widening or distortion of the carin is an indication of mediastinal involvemen to a degree that would prohibit a successfu resection As the surgeon gains experienc with bronchoscopic examination man more patients will be rejected for surgica therapy on the basis of bronchoscopic findings alone

QUESTIONABLE SIGNS OF INOPERABILITY

Signs of Extension Beyond Lung

Local invasion of neighboring tissues by direct extension *may not represent an absolute sign of inoperability unless some vital* structure has been *involved Paralysis of* the diaphragm on the involved side, *indica*

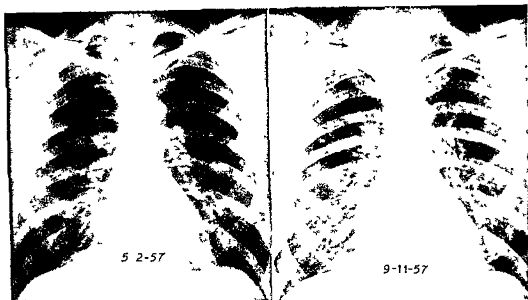


Fig 6a The lesion seen within the circle of the first rib on the right caused severe pain in the shoulder and arm of a 52 year old man

Fig 6b Four months later the lesion was seen to have enlarged Seven weeks following completion of irradiation therapy (3000 R) the lesion was surgically removed by an en bloc resection which included the apical segment and portions of the 1st 2nd 3rd and 4th ribs with intervening intercostal muscle bundles The neoplasm was found to have been converted into a fibrous mass by the irradiation therapy — making identification of cell type difficult

ing invasion of the phrenic nerve, is a questionable sign of inoperability, but since it is feasible to remove the pericardium along with the nerve and its accompanying vessels resection still might offer a chance of cure Direct invasion of the diaphragm may not preclude a successful resection The size of the tumor in such situations would play a large part in the decision as to whether or not surgery should be advised

Invasion of Chest Wall

Involvement of the chest wall by direct extension from a peripheral pulmonary neoplasm becomes an absolute sign of inoperability only when the involvement is of large dimensions or in such a position as to involve structures which cannot be excised surgically i e, aorta, brachial plexus, bodies of the vertebrae, etc Involvement of the first and second intercostal nerves is not a sign of inoperability if there is no gross invasion of the spine A localized area of invasion of the chest wall even when osteolytic destruction of ribs is evident does not necessarily preclude the possibility of an en-bloc resection of a portion of the chest wall along with the involved lobe (Fig 7)

Poor Pulmonary Function

Pulmonary emphysema and brochogenic carcinoma are two commonly associated diseases Severe degrees of pulmonary emphysema, which have already caused the patient to become a pulmonary cripple, may represent an absolute sign of inoperability In evaluating a patient from this standpoint, one will have to consider the overall pulmonary status in view of the extent of the resection that may be required Total pneumonectomy may be absolutely



Fig 7a The scapular shadow partially obscures the shadow cast by this neoplasm which has inv the chest wall of a 58 year old man Pain radiating along the third and fourth intercostal n to the anterior portion of the right chest was the presenting symptom

Fig 7b A roentgen film taken to show bony detail shows clearly the osteolytic destruction of tions of the 3rd and 4th ribs An en bloc resection including the right upper lobe and portion the involved 2nd 3rd 4th and 5th ribs adequately removed the lesion The muscles of the shou girdle protect the defect in the thoracic wall The patient is well and free of pain more than a following surgery

cated, but lobectomy and even segmental lobectomy might be tolerated with very little diminution of pulmonary function (Fig 8)

Age and Coronary Artery Disease

Age often has to be considered in determining whether or not surgery should be advised in the treatment of bronchogenic carcinoma Although the chronologic age may not be as important as physiologic age, it very often has to be considered since it may be directly associated with the patient's philosophy of living Many patients advanced in age chronologically with clear mental insight into the realities of life prefer not to be subjected to a major surgical ...re for the treatment of a malignancy On the other hand, many individuals beyond the age of 70 are well able to tolerate lobectomy and occasionally even total pn monectomy Physiologically, many patie having a bronchogenic carcinoma appear be much older than their chronologic a This may be an inherited characterist There is evidence, however, that excessi cigarette smoking may hasten the agi process, so that in addition to being a inciting cause for the bronchogenic carc noma, there has been a general deterioratio of the tissues of the body aside from th respiratory tract This is usually evidence by a sallow, unhealthy appearance, a la skin, premature graying of the hair, and general loss of vigor Very often the phy sician s first impression of the patient bein considered for surgery is that this man will not tolerate major surgery well This impression accompanied by other manifestations of the degenerative processes *such as*



Fig 8 Poor pulmonary reserve due to emphysema contraindicated total right pneumonectomy in this 70 year old man However right upper lobectomy was well tolerated One year following surgery he is comfortable and without sign of recurrence of the squamous call carcinoma

coronary artery disease and cerebal arteriosclerosis may well be sufficient to warrant the decision that surgery is inadvisable Many patients with a limited cardiac reserve tolerate surgery well and make uncomplicated recoveries However the presence of dyspnea any part of which can be ascribed to a failing heart would certainly contraindicate a pulmonary resection of the magnitude of a total pneumonectomy Chronic cardiac decompensation unrelieved by medical measures would make the advisability of pulmonary resection for bronchogenic carcinoma very questionable since the prognosis of the cardiac disease from the standpoint of time of survival may be poorer than that of the pulmonary neoplasm

SUMMARY

The surgeon must select carefully for surgical therapy patients having neoplasms suitable for resection

The salvage rate from the surgical treatment of bronchogenic carcinoma in the majority of patients is so low that little will be gained and much harm can result from an over aggressive surgical policy in selection of patients for surgery Survival rates following surgery for bronchogenic carci noma must take into consideration an

creased mortality and morbidity and an actual shortening of lives in the final results The authors agree with Maier[3] who states 'The little that might be gained by a very radical approach is more than offset by the high mortality and morbidity — that most *surgical cancer reports are lacking in a* broad viewpoint in that due consideration is not given to the debit side of the surgical balance sheet, namely, the lives of patients *in* reasonable comfort that have been shortened by high operative mortality resulting from ultraradical surgical procedures ' It is the responsibility of the surgeon to place into the equation his knowledge of the disease and its possible ramifications of the ability of the patient being considered to tolerate the proposed surgery, of the limitations of surgery and of the effectiveness of other therapeutic modalities Only then *can he arrive at the wise solution for the* problem presented by the individual patient

Through an appreciation of the biologic characteristics of the various types of bronchogenic carcinoma *it is possible to arrive* at a more critical selection of patients for surgery, a better choice of operative procedure, and improvement in survival rates

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Selection of Operation

BASED ON THE RATIONALE of treatment it is believed that lobectomy is the operation of choice in the surgical treatment of a patient having a bronchogenic carcinoma Total removal of a visceral organ which is the site of a primary neoplasm traditionally is the ideal surgical procedure This should include removal of the regional lymph nodes in an en bloc resection To state however that total pneumonectomy with dissection of the regional lymph nodes is the ideal operation for bronchogenic carcinoma does not mean that it is the operation of choice for the patient having a neoplasm of the lung

Pulmonary tissue is vital tissue and should be conserved as carefully as possible in a patient of any age Conservation of pulmonary tissue becomes increasingly important in patients in the age groups susceptible to primary neoplasms of the lung

Bugher[1] in a paper entitled Some Problems of Interpreting Statistics on Cancer Diagnosis and Treatment concludes It seems clear on reflection that survival time is not an adequate index of therapeutic efficiency There needs to be some measure of the quality of survival There is a great difference between the patient who manages

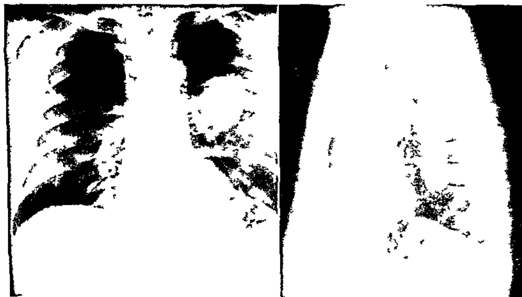


Fig. 1a & b Severe arthritis involving the ankles was the symptom that led to the detection of this large neoplastic mass in the left upper lobe The lesion was removed by left upper lobectomy which should permit a superior quality of survival without sacrificing time of survival The arthritis completely disappeared in two weeks following surgery

to survive as a suffering incapacitated and bedridden individual and one who although living for the same period of time is able to continue with normal or near normal activity for most or all of the period There is the implication in existing data that the therapeutic measures used may themselves be of such injurious character that the increasing life expectancy from eradication of the neoplasm may be partly or completely offset " To no other visceral organ of the body does this principle apply as clearly as it does to the lungs (Fig 1)

Review of the recent literature on the surgical treatment of bronchogenic carcinoma reveals that Brock[2] Ochsner,[3] and Gibbons[4] among others advocate the necessity of performing a total pneumonectomy Evaluation of their survival rates does not seem to bear out the prediction made by Graham[5] in 1948 that the routine performing of total pneumonectomy for cancer of the lung should yield a significantly higher five year survival rate as compared with survival rates in series of patients where selective resection is used when feasible Advocates of pneumonectomy, in advising a more radical surgical approach, are not able to achieve a higher rate of resectability as compared with those using selective resection The operative mortality following pneumonectomy ranges from 9 to 23 per cent according to various reports Surgeons limiting the extent of the resection when feasible generally have an over all surgical mortality under 10 per cent

Husfeldt[6] (an advocate of total pneumonectomy), working in Denmark where there are accurate vital statistics in a country with a uniform population and medical system, has shown that the over all five year salvage achieved by surgery is 5 per cent In the 1954 report[7] of 'Organized Clinical Investigation of Cancer' by the University of Michigan, 5 2 per cent of patients having cancer of the lung who were eligible survived five years Reports from other clinics in this country, in which there is undoubtedly some selection of patients in that those hopelessly ill when first diagnosed may not be referred for surgical evaluation show only a slightly better salvage rate from surgery The uniformity of these reports indicate that total pneumonectomy can achieve little more than lobectomy in completely eradicating the neoplasm and has the disadvantage of a significantly higher mortality and a poorer quality of survival There is no indication in the literature that the surgical skill of the individual surgeons reporting affects the survival rates once the patient has recovered from the operation The variations in surgical mortality rates are probably due to factors in selection of patients for surgical therapy and in post operative management

The objection to lobectomy in the treatment of bronchogenic carcinoma is that it does not allow an adequate mediastinal dissection This objection infers that pneumonectomy offers a better chance of complete cure by being able to remove all cancerous tissue Certainly in any operation for cancer the regional lymph nodes should be excised Johan Holst[8] in discussing the problem of gastric resection for malignancy asked the question "Just where do the regional lymph nodes end and the nodes of the general lymphatic system begin?" Because of the complex lymphatic drainage of the lungs within the mediastinum and the vital structures with which the nodes are in direct continuity (Fig 3, Chap III), for practical purposes the regional lymph nodes as far as the lungs are concerned are the peribronchial and hilar nodes These can be as easily removed with lobectomy as with pneumonectomy Likewise the corynal and peritracheal mass of nodes can be dissected and excised in performing lobectomy although the chance of affecting survival time if they are grossly involved with neoplasm is not great There is a great possibility in disecting within the mediasti

num, grossly involved with lymphatic spread of neoplasm, that barriers of resistance will be disturbed so as to lead to a more rapid and widespread dissemination of the cancer

The position of the neoplasm in respect to the point of section of the bronchus is the chief factor in determining the extent of resection The point of division of the bronchus should be at least 1 5 cm (Clagett et al) from visible or palpable evidence of neoplasm This factor is not a problem in removing peripheral neoplasms by lobectomy When the lesion has originated in a major bronchus of necessity a total pneumonectomy must be done unless a lobe or lobes can be preserved by performing a bronchoplasty Lobectomy will be feasible …ver in one-half of the patients suitable …rgical resection

…land has reported 2 cases of re…ce of carcinoma in the bronchial stump in a series of 21 patients following lobectomy for carcinoma He concludes from this that total pneumonectomy should be the operation of choice for patients having bronchogenic carcinoma and that a lobectomy should only be done as a compromise for consideration of pulmonary function He ignores the fact that there is at least a 6 to 10 per cent difference in the surgical mortality of lobectomy versus pneumonectomy so that at least 2 of the 21 patients treated with lobectomy would not have survived to have a recurrence if they had been subjected to total pneumonectomy Finally the 19 patients remaining are immeasurably more comfortable with lobectomy than they would have been if they had been deprived of the use of a total lung

The concept that less than total pneumonectomy may be an adequate operation for bronchogenic carcinoma is not new although opinions expressed in the literature on this subject have not stressed that lobectomy in the interest of conservation of pulmonary function makes it the operation of choice

Graham,[11] when he performed the first successful total pneumonectomy for bronchogenic carcinoma started the operation with the plan of limiting the resection to the left upper lobe It was only when the position of the lesion with respect to the major bronchus was determined that the courageous decision was made to remove the total lung It was fortunate that this historic operation was done on a patient having adequate pulmonary reserve permitting long survival with no apparent physical limitations This brilliant result unfortunately cannot be duplicated in a large body of patients having bronchogenic carcinoma because of their limited pulmonary reserve In many of these patients a more limited resection is well tolerated Graham,[11] although he was generally in favor of total pneumonectomy in the surgical treatment of bronchogenic carcinoma stated "There are cases in which it is worthwhile to take a chance on a lobectomy because of the horrible situation in which a patient may be left if total pneumonectomy is performed

Churchill[13] in 1937, in entering into the argument of lobectomy versus pneumonectomy compared the lymphatic system of the mediastinum to a 'swamp or a morass' and stated that under certain circumstances he elected to perform lobectomy for cancer In 1950 reporting the twenty year experience at the Massachusetts General Hospital with the surgical management of carcinoma of the lung he stated that he elected to perform lobectomy (1) When there was low pulmonary or cardiac reserve (2) when the diagnosis was in doubt (3) for small peripheral lesions without evidence of lymph node extension and (4) as a palliative procedure

Neuhoff and Aufses in 1948 concluded that "Lobectomy is a properly conceived operation that may be curative for circumscribed and peripherally invasive carcinoma of the lung ' They had no survivals for more than a year in patients discov

have extensive regional node involvement as shown by examination of the resected specimen In patients in whom the resected specimen revealed no lymph node involvement, a common factor causing death was blood borne metastases, a factor which is not affected by the type of operation

Robinson, Jones and Meyer[14] in 1956 reported the result of a survey they had made concerning the practice of thoracic surgeons in respect to selective resection in the treatment of bronchogenic carcinoma Seventy seven per cent of the surgeons queried stated that they perform lobectomy as an operation of choice under circumstances of their own choosing 40 per cent use it only as a compromise when there is some contraindication to pneumonectomy, and only six surgeons (2 per cent) stated that they consider lobectomy the operation of choice whenever it is anatomically feasible A frequent comment by surgeons answering the questionnaire dealt with the poor over all experience in attempting to cure pulmonary carcinoma This comment indicated that they were finding surgical therapy helpful to a limited group of patients and were searching for a method of improving results from surgery Experience indicates that this can be accomplished not by extending the limits of surgical excision by more radical procedures but by a careful selection for surgery of patients who can be benefited by resection

Insufficient pulmonary and cardiac reserve accounted for eleven of the seventeen surgical deaths following pneumonectomy and three of six deaths following lobectomy in our patients The high mortality from this cause in patients that have been carefully evaluated from the standpoint of their ability to tolerate the proposed resection further emphasizes the necessity of preserving pulmonary tissue whenever possible A ew of the patients who survived pneumonectomy are now completely incapacitated by their low pulmonary reserve The others, however, are leading active lives with only minor restrictions

SEGMENTAL RESECTION

Resection of a primary neoplasm of the lung by removing less than a lobe rarely is justified In certain patients, however a segmental resection may be an adequate procedure Very small pulmonary nodules due to a primary neoplasm located in the periphery of a segment in which there is no evidence of glandular involvement may at times be adequately removed by segmental resection Our longest survivor following resection is a woman now 76 years of age who 12 years ago had resection of an anterior segment of the left upper lobe



Fig 2 For three weeks this 64 year old woman noticed a streak of blood in the mucus she cleared from her throat each morning X ray revealed an abnormal shadow in the left upper lung field A small primary bronchogenic carcinoma was removed by resecting the anterior segment of the upper lobe The patient is alive and well twelve years later Six years before this x ray was taken an early carcinoma of the cervix was detected and cured by radium therapy Thus an intelligent patient aided by her alert physician has survived two separate primary carcinomas

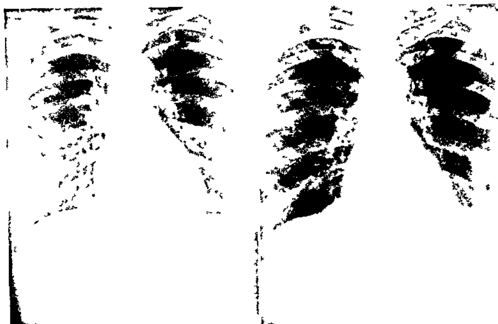
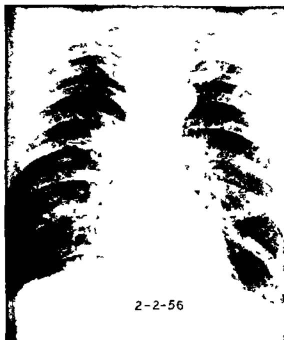


Fig 3a & b This small bronchiolar carcinoma was removed by segmental resection from the right lung of a 61 year old woman The two x rays taken four years apart were made as part of pre-employment examinations

for a small primary epidermoid carcinoma (Fig 2) Small bronchiolar carcinomas may be adequately excised by segmental resection (Figs 3a and b) Patients having poor respiratory function due to severe pulmonary emphysema who would otherwise be considered inoperable may tolerate removal of a segment of lung Patients who have previously had resections now occasionally present themselves for the problem of resection of an newly acquired lesion (Fig 4a and b) In such patients segmental resection may be feasible and may occasionally be an adequate operation Peripheral neoplasms (Fig 5a and b) which in addition require removal of a portion of the chest wall because of parietal invasion may be adequately excised in some instances by resecting less than the entire lobe The crux of the problem in these instances usually lies at the periphery of the lung and in the chest wall and not in the hilum It is recognized that it is undesirable to depart too widely from the traditional concept of the surgical treatment of neoplasm but individualization is important in the overall approach to this problem Segmental resection may be the operation of choice or the only procedure feasible in certain patients suffering from primary cancer of the lung

INDICATIONS FOR PNEUMONECTOMY

Pneumonectomy becomes necessary in approximately one half of patients having surgery for bronchogenic carcinoma due to the frequent location of the neoplasm in the major branch bronchi This is the most common site for the low grade epidermoid carcinomas Although the primary site may be relatively close to the lymph nodes at the hilum of the lung many of these lesions due to their biologic nature are locally invasive and slow to disseminate They seem to spread less commonly


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Fig 4a (*Page opposite—upper*) A right upper lobectomy was done to remove the pulmonary nodule casting the shadow in the x ray of the chest of a 70 year old man The lesion was a primary bronchogenic carcinoma—Squamous cell type

Fig 4b (*Page opposite—upper*) Nineteen months later a new nodule was seen to have developed in the lingular portion of the left upper lobe This lesion was removed by resecting the lingula and a subsegment of the anterior segment Pathologic study revealed this second lesion to be a new primary neoplasm The use of lobectomy in treating the original carcinoma permitted successful resection of the second lesion leaving the patient with an adequate breathing capacity for comfortable living

Fig 5a (*Page opposite—lower*) Peripheral squamous cell carcinoma (Pancoast tumor) involving chest wall and invading brachial plexus causing severe pain in upper chest shoulder and along the ulnar distribution to the right arm The neoplasm was removed by excising the apicoposterior segment of the upper lobe with an *en bloc* resection of portions of the involved ribs and bodies of the vertebrae

Fig 5b Appearance of chest one year following resection The patient is well without pain fifteen months following operation





blood stream Thus although due to their location in the bronchial tree, preservation of a portion of the lung is out of the question they may by being localized represent good lesions for surgical eradication An epidermoid carcinoma even when small (Fig 6a), by blocking a major bronchus may cause wheezing severe cough, and fever due to pneumonitis so that the patient seeks medical attention early Although the temporal factor is of secondary importance to the biologic factors concerned, time is nevertheless of great importance in this type of bronchogenic carcinoma so that resection may be applied while the lesion is still localized to the primary site

The finding of metastatic nodes in the hilum of the lung or in the mediastinum makes pneumonectomy the operation of choice This is true even though the primary tumor may be peripheral within the lobe There is little to be gained by removing a lobe when there is evidence that the neoplasm has extended along the lymphatic channels to lymph nodes beyond the involved lobe A radical pneumonectomy with excision of all accessible nodes is the operation of choice in this situation However, if pulmonary function must be considered a more limited resection may be preferable This may be followed by irradiation therapy over regions of known involvement (Fig 7a b and c)

BRONCHOPLASTIC PROCEDURES

Bronchoplastic procedures may be useful in selected patients in conserving pulmonary tissue in the treatment of bronchogenic carcinoma The use of this technique seems to find its greatest usefulness when used deliberately as an elective procedure conceived as an adequate cancer operation for the particular case being treated Thus, it should not be reserved for patients in whom total pneumonectomy is out of the question





Fig 6a This 74 year old man had cough and fever at the time this x ray was taken Penicillin therapy brought partial relief of symptoms but x ray shadow persisted He was still active seven years after left total pneumonectomy

Fig 6b Small bronchogenic carcinoma squamous cell type causing fibroid pneumonitis of left upper lobe





Fig 7a and b This squamous cell carcinoma arising in the periphery of the middle lobe was found at surgery to have metastasized to the hilar and subcarinal nodes Poor pulmonary function contraindicated total pneumonectomy

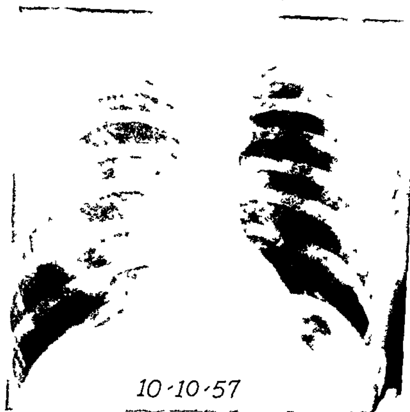


Fig 7c Appearance of chest fourteen months following resection of the middle lobe and involved nodes combined with irradiation therapy over mediastinum The patient is well and working almost two years following lobectomy

because of poor pulmonary function Where this procedure has been used in an attempt to extend the limits of surgery in performing a total pneumonectomy with resection of the lower trachea and coryna with anastomosis of the remaining bronchus to the trachea results have been disappointing as far as significant survival times are concerned Such an operation may, however provide palliation when no other treatment would be available

The right upper lobe bronchus and the superior segmental bronchus of the left lower lobe are two locations for neoplasms that customarily require a total pneumonectomy because of the proximity of the lesion to the main bronchus It is in these two locations where bronchoplastic procedures are of particular value

A neoplasm (Fig 8a, b and c) arising in the right upper lobe bronchus or its first order branches, even when the tumor is visible by bronchoscopy, may be adequately removed by upper lobe lobectomy including removal of the right main bronchus and a portion of the intermediate bronchus as *a sleeve resection* The remaining portion of the intermediate bronchus can then be anastomosed to the trachea at the region of the coryna In the patient who has survived longest (over five years) following a bronchoplastic type of resection for bronchogenic carcinoma in this location a wedge resection was employed without completely transecting the right bronchus (Fig 9) A bronchial leak occurred at the point of bronchial repair causing a complicating empyema which was drained by rib resection The patient subsequently made a good recovery although pooling of secre

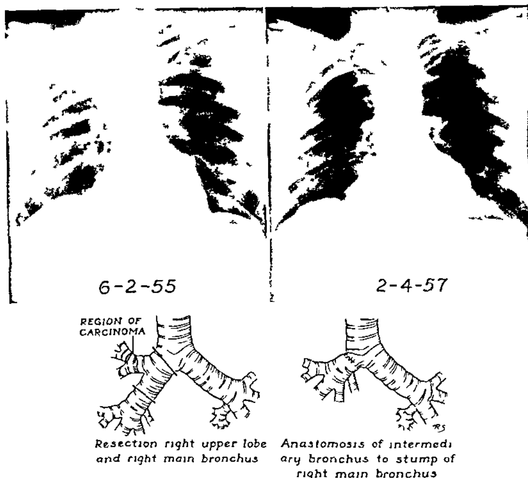


Fig 8a b and c A 48 year old man with obstructive pneumonitis due to localized epidermoid carcinoma of right upper lobe bronchus Resection of right upper lobe and right main bronchus preserving right middle and lower lobes Alive and well after two and one half years

tions in the kinked bronchus has been annoying Although this case represents a satisfactory survival complete transection of the bronchus with end to end anastomosis appears to give a better result with less morbidity We have used this type of anastomosis preserving the lower and middle lobes in seven patients

A well localized neoplasm arising in the superior branch bronchus of the left lower lobe because of its proximity to the left main bronchus would usually necessitate a left total pneumonectomy In certain of these cases the left upper lobe can be preserved by sectioning the left upper lobe bronchus just proximal to its bifurcation and sectioning the left main bronchus at approximately its mid point The remaining portion of the left upper lobe bronchus can then be anastomosed to the stump of the left main bronchus following the removal of the left lower lobe (Fig 10) We have employed this type of bronchoplastic procedure in four patients

Preservation of the right upper lobe was possible in three patients having epidermoid carcinomas extending into the intermediat bronchus In two patients a V plasty

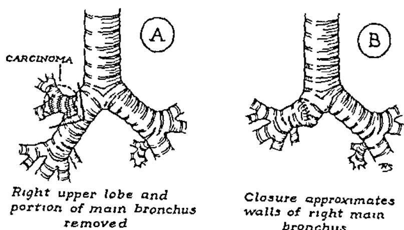


Fig 9

used to preserve the airway to the upper lobe (Fig 11) In the third patient the upper lobe bronchus was anastomosed to the side of the trachea after severing it from the right main bronchus which was completely resected The left lower lobe was preserved in two patients by performing a wedge resection and transverse closure of the bronchus after removing the left upper lobe

Bronchoplastic procedures were done on two patients who had right total pneumonectomies in a deliberate extension of the usual limits of resectability In both the airway to the left lung was preserved by an end to end anastomosis of the left bronchus to the trachea following resection of the right lung along with the coryna and lower trachea (Fig 12) One patient died on the twelfth postoperative day due to insufficient pulmonary function The other lived in reasonable comfort for one year before dying of carcinoma

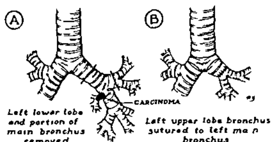
RESECTION FOR LESIONS OF UNPROVEN ETIOLOGY

The radical surgical approach to the treatment of bronchial neoplasms is capable of the greatest harm to the patient in the resection of a pulmonary lesion of unproven etiology Many benign lesions commonly found in the lungs are grossly indistinguishable from neoplasms Granulomas due to tuberculosis fungus infections, and lipoid pneumonitis may be particularly hard to differentiate from carcinoma by palpation and gross inspection Even the pathologist with the limitation of frozen section technique may be capable of error in diagnosing lesions sent to him at the time of surgery

Peripheral lesions of unknown etiology should first be resected as tumor biopsies or by segmental resection and sent to the pathologic laboratory for diagnosis If a diagnosis of neoplasm is established a more extensive resection may be indicated Bronchiolar carcinomas when small may be adequately removed by segmental resection Neoplasms of other types generally require lobectomy unless involved hilar nodes are present indicating total pneumonectomy The surgeon must consider not only the nature of the lesion but the patient s total economy in deciding the extent of resection desirable

Hilar lesions obstructing major bronchi and accompanied by distal suppuration may be very difficult to identify histologically Incising into the lesion to obtain adequate tissue for identification is often technically difficult and may involve injury to major structures committing the surgeon to a more





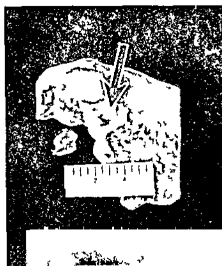


Fig 10 A 47 year old man with history of recent pneumonitis which cleared with antimicrobial therapy Bronchoscopy and bronchography revealed a tumor and notching of lower lobe bronchus. Resection with bronchoplastic procedure for a small localized undifferentiated carcinoma Survived four years

extensive resection than desirable Bronchotomy at a point proximal to the obstructing lesion often is helpful in establishing the diagnosis without committing the surgeon to an extensive resection Broncholiths mucoid impactions impacted foreign bodies and lipoid granulomas all may simulate a hilar carcinoma Bronchial adenomas also should be differentiated from bronchogenic carcinoma since they generally can be removed by partial resections if the distal pulmonary tissue has not been irrepar

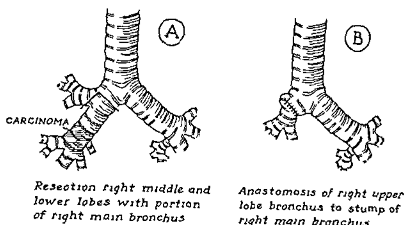


Fig 11

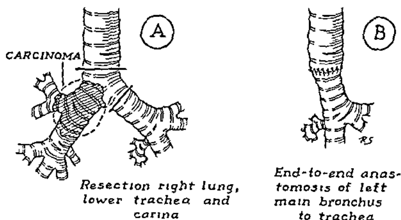


Fig 12

damaged The importance of conservation of pulmonary tissue cannot be overemphasized *When dealing with neoplasm radical* surgery often is mandatory and the risks are justified These same radical measures and risks, *however, should not be imposed upon* patients having lesions of unproven etiology that may represent little or no threat to the patient's life or health It is just as reprehensible to remove an entire lung for a benign lesion causing no symptoms because of a mistaken idea that it is a neoplasm as to remove an arm or a leg because of the *presence of a benign tumor*

PALLIATIVE RESECTION

There is a definite place for pulmonary resection for the purpose of affording palliation of unpleasant symptoms in patients *having bronchogenic carcinoma In apply*ing the principle of palliative surgery, however, the surgeon should keep in mind that *one cannot palliate a patient who has no* symptoms or only vague symptoms It is not possible to predict accurately the symptoms that will be experienced in the future by a patient having a bronchogenic carcinoma The loss of pulmonary *function due* to the resection may cause far more distressing and disabling symptoms than would *have been experienced* by the patient if the disease had been allowed to run its normal course without interference by surgery *Similarly,* imprudent palliative attempts

may actually shorten survival time by overly aggressive interference with the lymph node barrier and dissemination of the carcinoma

Palliation can seldom be afforded by resection of the primary carcinoma when distant metastases are already evident The metastases may cause the more aggravating symptoms and be the determining factor in the survival time Pulmonary resection as a palliative procedure must be justified by an attempt to control distressing symptoms already in evidence The most common symptoms that can be relieved by surgery are hemoptyses toxicity from suppuration cough and pain

Hemoptysis Hemoptyses due to bronchogenic carcinoma are rarely severe Typically the neoplasm ulcerates within the bronchial lumen causing small amounts of blood to be mixed with the expectorated bronchial secretion If however the neoplasm erodes into a major pulmonary vessel a quickly fatal hemorrhage can result Hemoptyses due to bronchial adenomas are frequently severe and may cause death by flooding of the tracheobronchial tree Usually the indication for pulmonary resection specifically to control coughing up of blood occurs in the peripheral type of carcinoma that has undergone central necrosis resulting in abscess formation The patient having such a lesion is plagued by a persistent cough productive of foul bloody sputum At times the amount of blood coughed up may be alarming In such a situation resection may be of great value in eliminating the cough and the hemoptysis even though the resection is not curative

Suppuration Suppuration beyond a bronchial neoplasm that has caused abscesses and irreparable damage to the involved lung is an indication for pulmonary resection even though cure may not be possible It must be borne in mind that the obstruction and suppuration of recent origin at times can be more easily relieved by irradiation over the obstructing neoplasm combined with antimicrobial therapy Attempts to effect palliation by the total removal of a lung when the point of bronchial section traverses neoplasm will frequently lead to a bronchial stump leak and a complicating empyema This complication frequently makes the patient more uncomfortable and may lead to a shorter survival period than if the lung had not been removed Although in general the results of palliative resections are usually disappointing the rapid although temporary improvement following resection of a destroyed suppurating lobe or lung distal to a bronchial neoplasm may be most gratifying

Cough Severe cough due to a bronchial neoplasm that cannot be relieved by irradiation therapy and by the use of opiates occasionally becomes an indication for a palliative resection A persisting unrelenting cough especially when it appears in exhausting paroxysms may greatly weaken the patient and make it impossible for him to get adequate rest Pulmonary resection even though it is known that it cannot be curative may be justified in such a situation It has been observed that if at the time of the attempted resection it is found that the procedure will be unduly hazardous due to the involvement of major pulmonary vessels or major bronchi that severing branches of the vagus nerve below the recurrent laryngeal nerve will often afford palliation of this symptom

Pain Relief of pain by excising a neoplasm which has invaded parietal structures may be an indication for a palliative resection Peripheral cancers of the lung may attach themselves to the chest wall invading the pleura and eventually infiltrating intercostal nerves This will cause a severe unrelenting type of pain which radiates along the nerve pathways Even though there may be preoperative evidence of spread of the disease beyond the limits of resection

lobectomy or segmental lobectomy along with resection of the chest wall involved may give prolonged relief from pain

Neoplasms involving the superior sulcus of the chest which invade the first and second intercostal nerves producing pain along the distribution of the ulnar and brachio cutaneous nerves can be removed surgically without producing structural disability Resection of a lesion which has more extensively invaded the neural roots of the brachial plexus may be of temporary value as a palliative procedure, although there will be permanent neurologic defects in the arm and hand on the involved side Chardack and MacCallum[17] have reported a five year survival without evidence of recurrence of carcinoma following a combination of surgical excision and x ray therapy in such a lesion

Occasionally a peripheral lesion in the lower lobes will involve the diaphragm causing pain in the shoulder Excision of the lobe along with a portion of the diaphragm is a feasible surgical procedure that may give relief of pain even though cure cannot be effected

PALLIATIVE SURGERY OTHER THAN RESECTION

Palliation of symptoms may be possible in situations where exploratory thoracotomy and resection of the neoplasm is not feasible or is inadvisable Lesions that have invaded the phrenic nerve or diaphragm may cause severe pain in the shoulder In terruption of the nerve above the neoplasm will relieve this pain Intercostal neurectomy may be of great help in relieving pain due to a peripheral neoplasm that has invaded the chest wall so extensively that resection is not feasible Pleurectomy is useful in preventing the accumulation of pleural fluid when the pleural surfaces are studded with neoplastic implants While none of the above procedures might offer enough palliation to in themselves justify thoracotomy they should be kept in mind and applied in suitable cases when thoracotomy has been done to determine the possi bility of successful resection or to establish diagnosis

Evaluation of Palliative Surgery. Palli ative resections in alleviating symptoms caused by bronchial neoplasms are difficult to evaluate from the standpoint of increas ing survival time They cannot be judge in retrospect unless the surgeon has statec in the record at the time of surgery that the resection was done for palliation and not for cure The concept of palliative resec tions must not be used to justify the per formance of a resection in situations where it cannot conceivably prolong life and alleviate suffering merely because it is te nically feasible Smith[14] recently (195 reported on the results of raising the resec ability rate in operations for cancer of th lung Alarmed by the high mortality o exploratory thoracotomy in nonresectable cases of cancer of the lung he determined to carry out a palliative resection in every case in which surgery was undertaken He achieved a resectability rate of 97 2 per cent in 147 cases Forty eight of thes resections were deemed to be palliative i that known neoplasm was left behind in the course of the resection The survival of these 48 patients was carefully evaluated from the standpoint of time and relief of symptoms The operative mortality in this group was 21 per cent Of the remaining 38 patients 19 patients survived eigh months and 14 survived one year Bignall in analyzing the survival rate of 255 un treated patients found that one half of these patients survived nine months In discussin palliation Smith pointed out that pneumon ectomized patients usually have a short terminal illness — a doubtful dividend of surgical palliation Smith states that 'the results in the later period were very mucl worse than those of the first half of the series and this may be explained by the

inclusion, not deliberately, of a number of cases in the later period which would have been excluded earlier This tendency to increase the scope of operation beyond the accepted indication seems in all respects undesirable " Smith found palliative resections most useful in relieving hemoptysis, cough, and the effects of suppuration but less useful in relieving pain

Exploratory Thoracotomy. Exploratory thoracotomy for the purpose of establishing the diagnosis of neoplasm in situations where the clinical evidence indicates non resectability is justified under certain circumstances It should be recognized, however, that such a thoracotomy carries a definite mortality, inevitably adds to the morbidity, and may shorten survival time Boyd[10] reports an 8 6 per cent hospital mortality for exploratory thoracotomy in nonresectable cases of carcinoma In Ochsner's series[11] the mortality was 18 per cent Taylor[12] (1954) found that 31 per cent of patients died in three months following exploration for carcinoma when resection was not feasible The appreciation of the harmful effects of exploration seems greater among lay people than by the medical profession The fear is often expressed by patients that surgery will "spread the cancer " This fear is not wholly ungrounded and it is the responsibility of surgeons to eliminate as much as possible explorations that are of doubtful value to the patient

There is an understandable reluctance mong radiologists to treat a lesion not istologically proven to be neoplasm In ıe interest of accurate reporting of results therapy such confirmation of diagnosis is ghly desirable However, the harm resulting to the patient with nonresectable bronogenic carcinoma, especially if medianal involvement has caused tracheal or vena caval obstruction, should prohibit exploration The beneficial results that might be expected from irradiation therapy are probably more than offset by the harm done by the exploration both in respect to morbidity and mortality

Exploratory thoracotomy for diagnosis in patients having lesions that are obviously not resectable should not be advised until every other diagnostic procedure that might provide suitable tissue for examination has been carried out i e , bronchoscopy, cervical mediastinal node biopsy, needle biopsy, examination of sputum and available pleural fluid for neoplastic cells Exploratory thoracotomy in patients in whom pathologic proof of bronchial neoplasm has been obtained and who have lesions obviously nonresectable has only the dubious value of proving that surgical resection is impossible

SUMMARY

1 Lobectomy when feasible is the operation of choice in treating the patient having bronchogenic carcinoma

2 Pneumonectomy will be necessary i approximately one-half of patients havin a malignant bronchial neoplasm because o the location of the lesion and the presence of lymph node metastases

3 Bronchoplastic procedures in the interest of preservation of pulmonary tissue find a useful place in the surgical treatment of carcinoma of the bronchus

4 Palliative resection is justified to relieve unpleasant symptoms Hemoptyses, cough, effects of suppuration, and pain may all be palliated by surgery

5 Exploratory thoracotomy in the incurable patient is accompanied by an inevitable morbidity and a significant mortality It is justifiable, however in borderline cases to establish the fact of nonresectability a at times to obtain histologic proof of diagnosis when this information can obtained by a lesser procedure

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Irradiation Therapy

Irradiation therapy occupies a major role in the treatment of bronchogenic carcinoma Only one third of the patients with this disease have surgically resectable lesions and less than 10 per cent can be cured by surgery due to the biologic characteristics of the neoplasm and the difficulty of detecting it when still in a localized state Many of the remaining patients become candidates for irradiation therapy This modality of treatment is capable of modifying the natural history of the neoplasm to bring about relief of distressing symptoms in many patients and an apparent cure in an occasional case Studies of survival curves comparing untreated patients with those receiving irradiation therapy indicate that in the majority of patients receiving therapy survival time is not increased (Fig 11) In the series receiving therapy however there will be a small percentage of patients surviving beyond the fifth year while in untreated patients rarely will a patient live more than three years following onset of symptoms The value of irradiation therapy is chiefly in its role of palliation so that this therapy must be kept in mind in the management of patients having bronchogenic carcinoma

The role of irradiation therapy in the treatment of bronchogenic carcinoma is being presented by the authors from the viewpoint of the thoracic surgeon and physician responsible for the direct care of the patient rather than from that of the radiologist No attempt will be made to present technical details of the actual application of irradiation therapy Likewise no comparison will be made of the effectiveness of irradiation therapy given by the standard therapy units as opposed to the cobalt 60 and supervoltage units Choice of the method by which the patient is treated rests properly in the hands of the radiologist who understands the technical advantages of one unit over the other in the management of the particular patient to be treated Consideration of total dosage and fractionization of the dose into individual treatments is also the prerogative of the radiologist The physician or surgeon responsible for the care of the patient should have a knowledge of the value and also the limitations of irradiation therapy so that he will refer to his radiologic consultant patients presenting pathologic aspects of the disease in which irradiation therapy may be helpful

Irradiation therapy involves the use of a physical agent very real though unseen that is capable of destroying living cells In its use side effects that may be unpleasant must be accepted Although the total dosage used will vary according to the aim of therapy and the character of the normal tissues that may be affected an aggressive attitude should be the rule if benefit is to be expected It is incongruous for a surgeon who accepts a patient for surgery with little thought of the ordeal of surgery incisional pain and weeks of morbidity to withhold irradiation th[...] becau[...] [...]asant side effects,

should a surgeon who removes an entire lung with equanimity be disturbed by irradiation fibrosis? An over radical attitude which may reach a point of diminishing returns and increasing harm, whether it be surgical therapy or irradiation therapy is to be avoided Once chosen however the modality of irradiation therapy should be employed with a vigor consistent with the ultimate welfare of the patient

Irradiation therapy has been reserved in general for patients having bronchial neoplasms not suitable for surgical excision Before 1933 when pulmonary resection was demonstrated as feasible in the treatment for bronchogenic carcinoma patients had been treated exclusively by means of irradiation therapy Diagnostic measures during that period were not sufficiently developed to allow frequent detection of a localized bronchial neoplasm Since disseminated carcinoma was being treated the results were disappointing and irradiation therapy was judged to be of little value It is fair to pose the question as to whether irradiation therapy would be as effective as surgical excision in patients having localized bronchial neoplasms This question will probably never be answered since no one may have the courage deliberately to withhold surgical excision from patients with favorable lesions An occasional patient with such a lesion who refuses surgery (Fig 1a b c d) or whose pulmonary function contraindicates surgery (Fig 6a and b) becomes available for irradiation therapy Results of irradiation therapy in this group suggest that this modality may be curative to a greater extent than most physicians realize The major obstacle to determining the effectiveness of cancericidal doses given to localized peripheral bronchial neoplasms is the

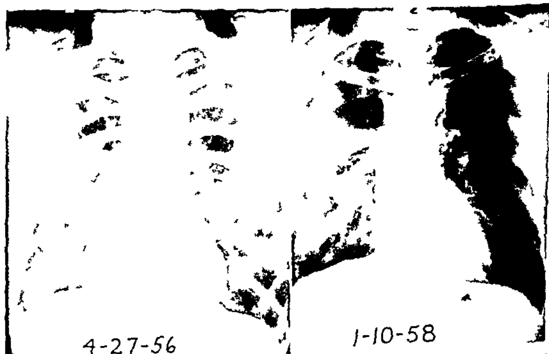


Fig 1a X ray of a 60 year old man who was found at bronchoscopy to have a small epidermoid carcinoma obstructing the bronchus to the superior segment of the right lower lobe He refused to have surgery Irradiation therapy was given over the obstructing neoplasm

Fig 1b Twenty one months later x ray of chest shows minimal scarring at site of previous pneumonitis and pulmonary abscess Patient is well and without symptoms

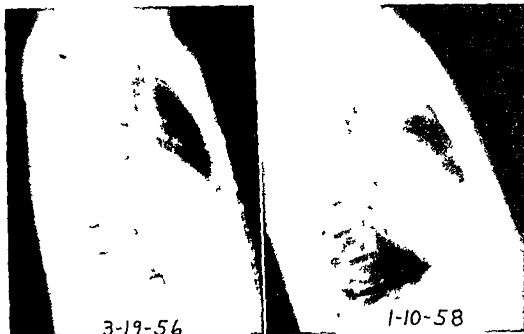


Fig 1c Right lateral projection showing abscess in superior segment of lower lobe beyond obstructing carcinoma

Fig 1d Twenty two months later only minimal scarring remains

difficulty of obtaining histologic proof of such lesions without surgical exploration and biopsy Due to this factor surgery will probably remain the treatment of choice for localized neoplasm originating in the lung while irradiation therapy will be used for inoperable and non resectable lesions recurrences following surgery and metastases

IRRADIATION THERAPY IN RELATION TO CELL TYPE

The response of a neoplasm to irradiation is governed largely by its cell type Highly undifferentiated tumors are very responsive to irradiation therapy Well differentiated epidermoid carcinomas fall in the median scale of responsiveness to irradiation Adenocarcinomas including the bronchiolar type and the cylindromatous type of bronchial adenoma respond very little to this type of therapy

The value of irradiation therapy to the patient however may be influenced less by the cell type of the neoplasm than by its degree of localization The patient having a highly undifferentiated bronchogenic carcinoma of the small round cell type almost always has a widely disseminated neoplasm by the time the diagnosis is established Although irradiation therapy may be useful in temporary control of symptoms due to the primary lesion or metastases that retrogress quickly following therapy the patient rarely survives for more than a few months

In spite of its greater resistance to the effects of irradiation the well differentiated squamous cell carcinoma by virtue of its tendency to remain localized for a longer period of time is the most favorable lesion for irradiation therapy The influ biologic characteristics of the tains just as surely to the tion therapy as it does t surgery

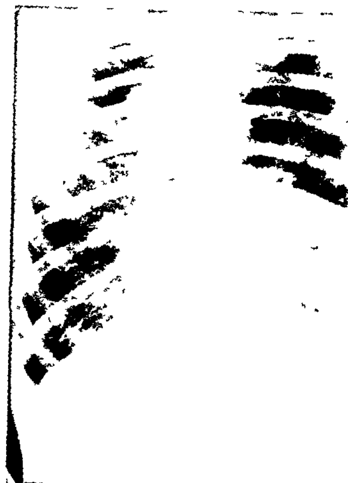


Fig 2a Squamous cell carcinoma which at was found to be nonresectable because of inv vertebrae

INDICATIONS FOR IRRADIATION THERAPY IN INOPERABLE AND NONRESECTABLE PATIENTS

Inoperable and nonresectable patients having malignant bronchial neoplasms not suitable for surgical excision make up the largest group for whom irradiation therapy is indicated The usual contraindication to resection is evidence of extension of the eoplasm beyond the site of origin This ay be manifest by direct extension to a structure that it is not feasible to resect along with the neoplasm, i e , aorta, esophagus, trachea, spine, etc (Fig 2a, b) In this event the neoplasm may be well local-

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Fig 2b Appearance of chest six months following irradiation therapy There has been complete disappearance of the severe pain that was the presenting symptom This 46 year old man feels well and is working one year following therapy

the neoplasm these studies along with the clinical picture presented by the patient often permit an accurate diagnosis of bronchogenic carcinoma These patients should be treated with irradiation therapy without being subjected to exploratory thoracotomy The risk of exploratory thoracotomy for a nonresectable bronchogenic carcinoma outweighs the benefits derived from it

Mediastinal Invasion

Invasion of the mediastinum by direct extension or by metastases to lymph nodes is a common sign of inoperability Signs of superior vena caval obstruction tracheal compression and involvement of the recurrent laryngeal nerves are indications of mediastinal extension Histologic proof may be obtained from bronchoscopic examination or from a cervical or high mediastinal lymph node obtained by means of cervicomediastinal exploration Even though histologic proof is not easily available irradiation therapy in combination with chemotherapy should be used Patients having gross swelling of the neck and arms and those dyspneic due to tracheal compression should be treated initially by means of chemotherapy This type of therapy produces shrinkage of the neoplasm without the initial swelling that may follow the first treatments with irradiation therapy It may be safe to proceed cautiously with irradiation two to three days following the i



Fig a Squamous cell carcinoma which at exploratory thoracotomy was found to be nonresectable because of invasion of the bodies of the vertebrae

INDICATIONS FOR IRRADIATION THERAPY IN INOPERABLE AND NONRESECTABLE PATIENTS

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Fig 4a Exploration of the left chest of this patient revealed a pulmonary neoplasm was nonresectable because of invasion of the aorta and esophagus

Fig 4b Six months later the neoplasm had greatly enlarged Irradiation therapy was given A tumor dose of *approximately 4000 roentgens was given through four 15/15 cm ports in a period of 20 days* using 220 KV equipment

Fig 4c X ray of chest six years later Patient is well working and without sign of recurrence of the neoplasm almost eight years following irradiation therapy

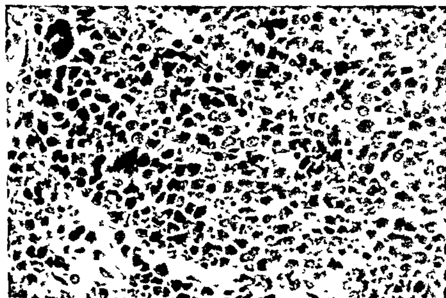


Fig 4d Biopsy revealed an anaplastic carcinoma containing large pleomorphic tumor cells Hematoxylin and eosin X700

tion of chemotherapy *As a rule patients* with mediastinal involvement respond well to irradiation therapy and obtain welcome relief from distressing symptoms (Fig 5) It is true that the period of relief may be *transient but we have observed one patient* who lived over two years following irradiation over a proven bronchogenic carcinoma causing severe vena caval obstruction This patient was free of symptoms and worked

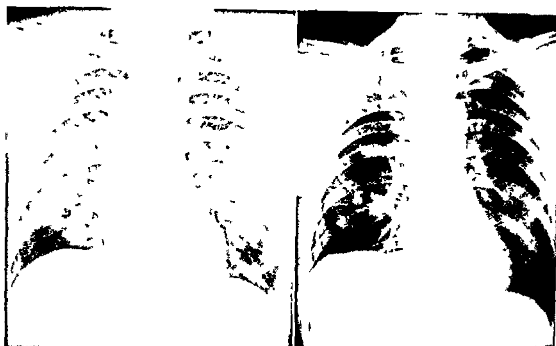


Fig 3a X ray 1 15-46 This 54 year old man whose chief complaint was pain in right shoulder was found at exploratory thoracotomy to be nonresectable because of a neoplasm arising in the right upper lobe bronchus which had invaded the phrenic nerve and lower trachea Biopsy revealed squamous cell carcinoma

Fig 3b X ray 4 1-46 Two and one half months following x ray therapy hilar mass almost completely disappeared This man survived seven years without sign of recurrence and died of an unrelated cause A tumor dose of approximately 3000 roentgens was given through four ports over a period of 20 days using 400 KV equipment

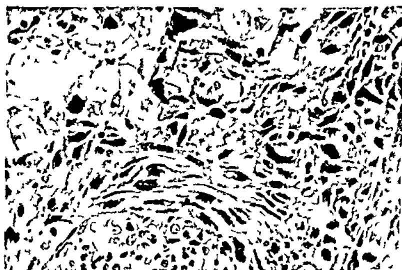


Fig 3c Photomicrogram of neoplasm showing pleomorphic spindle shaped and giant tumor cells in epidermoid carcinoma Hematoxylin and eosin X700



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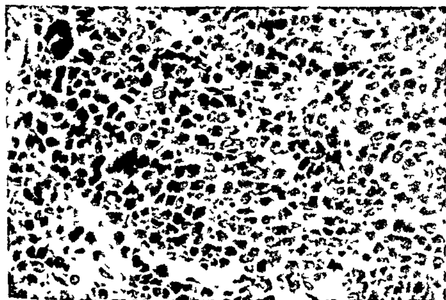


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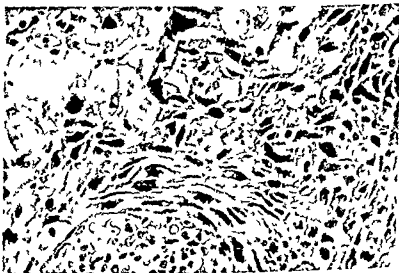


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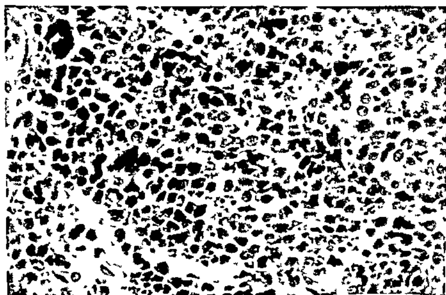


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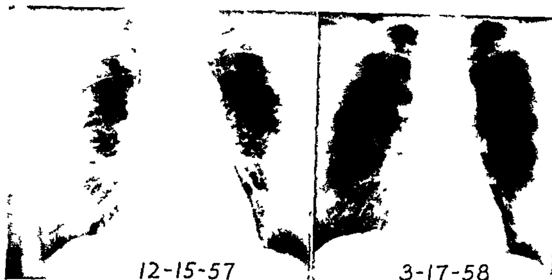


Fig 5a This 69 year old man had gross swelling of the neck shoulders and arms due to vena caval compression and wheezing respirations due to tracheal narrowing caused by mediastinal invasion of a bronchogenic carcinoma arising in the right upper lobe

Fig 5b Four months following irradiation therapy using 2 MEV equipment delivering 3500 roentgens to the tumor area The patient is completely free of symptoms The swelling of the neck and arms is no longer present

actively during eighteen months of this period

Pleural Effusion

The presence of pleural effusion complicating a bronchogenic carcinoma may contraindicate the use of surgical therapy An absolute contraindication exists if neoplastic cells are demonstrated in the fluid Irradiation therapy may be helpful however, in the management of a patient having this sign of extension of the neoplasm Roentgenograms of the chest following aspiration of the fluid may reveal a shadow producing localized mass within the involved lung In this situation the neoplasm has probably broken through the pleural barrier and is shedding neoplastic cells into pleural space to cause the effusion Irradiation therapy given over such a neoplasm may induce regression or quiescence in growth and bring about clearing of the pleural effusion Effusions secondary to venous obstruction due to neoplasm may also clear temporarily following therapy over the involved hilum Pleural effusion due to extensive neoplastic implants on the entire visceral and parietal surfaces presents a problem of too great an area of involvement to be treated easily with irradiation therapy alone The instillation of radioisotopes or nitrogen mustard compounds into the pleural cavity in such cases is helpful in delaying the formation of the pleural fluid and in some cases causes obliterative pleuritis sufficient to prevent further accumulation of fluid Irradiation therapy may be combined effectively with chemotherapy in many patients having malignant pleural effusions secondary to bronchogenic carcinoma

Distant Metastases

Patients who are inoperable because of the obvious presence of distant metastases may receive benefit from combinations of irradiation and chemotherapy Irradiation like surgical therapy can be effective in prolonging survival time only when it is applied to a localized lesion It may quite effectively control the primary lesion treated

in a patient who finally succumbs to wide spread metastases Irradiation over hilar masses may relieve cough or hemorrhage and open obstructed air passages Pain due to invasion of parietal structures is often relieved following irradiation therapy Chemotherapy may be used later or con comitantly in an attempt to control the distant meastases The fact that such meta stases are present should not deter one from use of irradiation for palliation of symp is unless it is felt that life expectancy is te short

INADEQUATE PULMONARY AND CARDIAC FUNCTION

Severe diminution of respiratory function or cardiac disease may prohibit resection and even exploration in patients whose chest roentgenograms reveal obvious broncho genic carcinomas (Fig 6) Irradiation therapy should not be withheld from these patients merely because of the lack of histo logic proof Inclusion of these patients with unproven diagnosis in a reported series treated with irradiation therapy for carcin oma would undoubtedly be challenged In the interest of accurate reporting the results of therapy in these patients may be reported separately from the results in proven cases

FOLLOWING RESECTION

Irradiation therapy may be indicated fol lowing resection of the primary lesion if

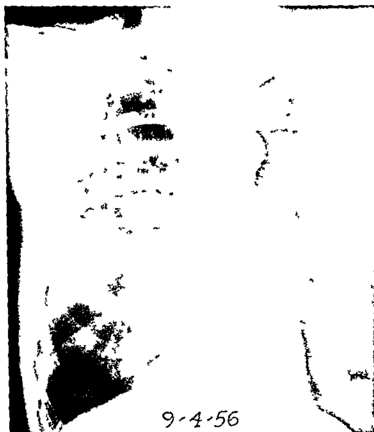


Fig 6a This 66 year old male patient was severely crippled by poor pulmonary funct on due to b lateral pulmonary emphysema Even lobec tomy for removal of the bronchogenic carcinoma in the right upper lobe was considered inadvisable



Fig. 6b. One year following irradiation therapy there is little remaining evidence of the neoplasm. The patient was still alive twenty months following therapy.

gross neoplastic tissue is knowingly left behind or if there is the probability of an incomplete resection in the proximity of the neoplasm. Irradiation therapy over the region of known or suspected involvement may be helpful in retarding the extension of the neoplasm. Silver clips applied at surgery to outline the area of known involvement will be helpful to the radiologist in accurately applying therapy. However, the results of irradiation therapy for this type of indication is particularly discouraging. There is presumptive evidence that dissection in masses of neoplastic nodes or disturbance of the lymph channels beneath the pleura may break down barriers of resistance and encourage rapid dissemination (Fig. 7). Judgment is required at the time of surgery in borderline cases of resectability as to whether resection should be attempted, since often irradiation alone will be much more effective than resection followed by irradiation over remnants of neoplasm.

IRRADIATION FOR LOCAL RECURRENCE FOLLOWING RESECTION

Evidence of residual malignancy may later develop following resection. *In the* majority of patients this will occur within a period of two years. Reoperation even for a well localized recurrence rarely is feasible. Irradiation therapy, however, may be beneficial if the area of the recurrence is of such

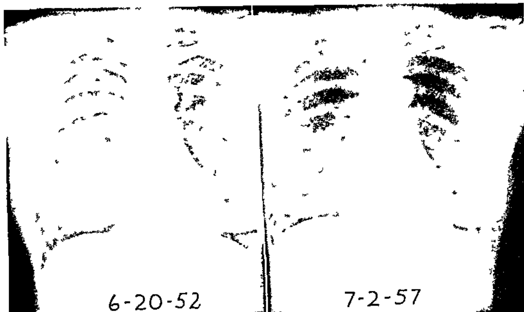


Fig 7a The presence of the pulmonary nodule in the right upper lobe of this 72 year old woman was thought to represent no threat to her health

Fig 7b Over 5 years later the nodule has greatly enlarged but still caused no symptoms At operation an epidermoid carcinoma was found that was attached to the parietal pleura Right upper lobectomy was carried out along with resection of the involved pleura

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Fig 7c Two months following resection the chest appears clear

Fig 7d Five months following resection there was evidence of rapid growth of the neoplasm in chest wall The patient had severe pain in the right shoulder and arm Dissection in the extr plane involved with neoplasm accelerated the growth of the lesion probably brought on symptoms and hastened death Irradiation therapy following surgery gave no benefit surgery it might h eat value

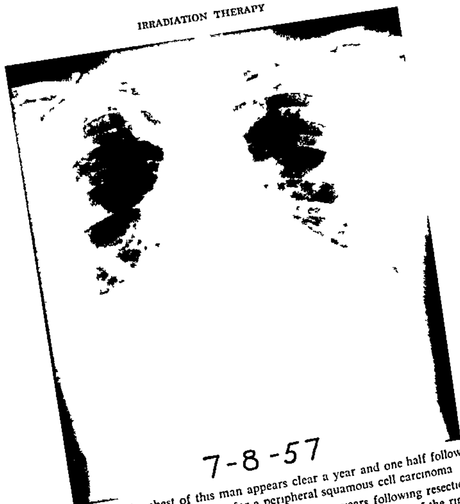
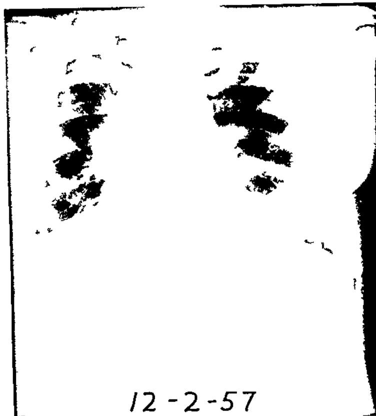


Fig 8a The chest of this man appears clear a year and one half following right upper lobectomy for a peripheral squamous cell carcinoma

Fig 8b (*Page opposite — upper*) Almost two years following resection there is evidence of recurrence of the neoplasm in the hilum of the right lung The patient had developed a harrassing cough and complained of pain Positive confirmation of recurrent neoplasm was obtained from examination of a node removed from the right cervical fossa

Fig 8c (*Page opposite — lower*) Four months following irradiation therapy the neoplasm has regressed Pain and cough were completely relieved

size as to be easily encompassed by a relatively small field so that a cancericidal dose can be delivered to the neoplasm This opportunity for temporary control of residual neoplasm occurs most often when the resection has been limited to a lobectomy since the presence of air containing pulmonary tissue within the hemithorax allows radiographic detection of the recurrence (Figs 8 9 and 10) Following total pneumonectomy recurrence within the hemithorax may be suspected but cannot be localized accurately enough to permit irradiation therapy unless it can be detected bronchoscopically in the trachea or bronchial stump Irradiation therapy over locally recurrent neoplasm may alleviate cough bloody expectoration pain and vena caval obstruction thus permitting a more comfortable quality of survival Its availability as therapy does much to encourage the patient in spite of the knowledge that the dreaded cancer has returned


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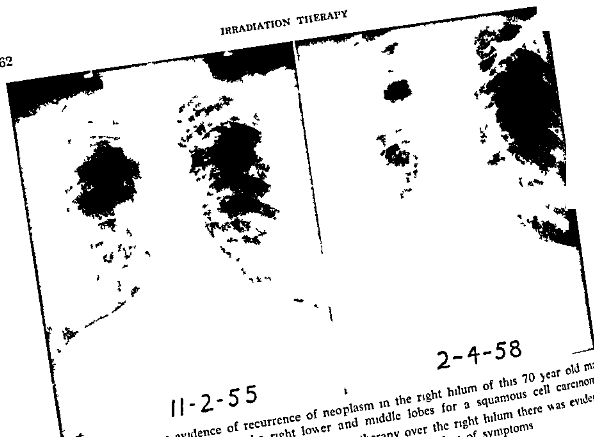
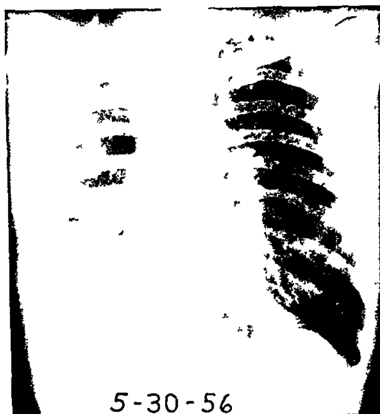


Fig 9a There was evidence of recurrence of neoplasm in the right hilum of this 70 year old ma one year following resection of the right lower and middle lobes for a squamous cell carcinom
Fig 9b Over two years later following irradiation therapy over the right hilum there was eviden of radiation fibrosis but the patient was well and free of symptoms

IRRADIATION THERAPY PRELIMINARY TO RESECTION

The value of irradiation therapy as a preliminary treatment to resection has not been fully explored Irradiation over neoplasms that have invaded main bronchi in close proximity to the carina may cause the tumor to recede so that a patient at first considered inoperable becomes a suitable candidate for resection later Cleland in 1949 began studying preoperative irradiation therapy combined with resection This study was prompted by an experience in which a patient under his care deemed inoperable because of the bronchoscopic findings of carcinoma close to the carina and subcarinal widening became resectable four months following a radical course of irradiation Examination of the right lung following resection failed to reveal macroscopic or microscopic evidence of tumor The patient died two years later due to metastases Fifty patients thought to have neoplasms localized to the primary site were given irradiation therapy and at a later date 24 of these had total pneumonectomies Twelve of the 50 patients were deemed inoperable because of bronchoscopic findings Five of the 12 subsequently had total pneumonectomies One died later from a recurrence in the stump but the other four were doing well at the time of the report Cleland found the operative difficulties no greater in thes patients than in untreated cases Lindsko has recently reported 2 patients who wh first evaluated for surgery were deem inoperable because of the bronchosco findings of neoplasm within a centim of the carina Following irradiation ther the airway opened and atelectasis was relieved Subsequent bronchoscopic examination revealed a normal bronchus with no



F g 10a X ray of chest show ng sat sfactory cond t on s x months follow ng resect on of the r ght lower and m ddle lobes for a squamous cell carc noma n the bronchus to the super or segment of the lower lobe

visible carcinoma Both then were subjected to left pneumonectomy One patient is alive and well four years following resection and the other has survived over a year without sign of recurrence Obviously this combination of therapy is of value only when there is no evidence of extension of the disease beyond the area encompassed by the irradiation therapy and in the presence of a favorable cell type

Irradiation therapy preliminary to resection may be even more useful when used over peripheral carcinomas that have invaded the chest wall Lesions in this location often remain localized to the site of origin for a long period of time They do however invade the lymphatic channels in the endothoracic fascia and microscopically the extension may be far more extensive than indicated by macroscopic evidence This explains the rapidly distressing painful recurrence of carcinoma in cases where the dissection in the extrapleural plane breaks across these involved lymphatics during resection of a lobe or lung (Fig 7) Unless a wide en bloc resection of the chest wall and involved lung is employed the result of surgery in this group of patients is unrewarding These cells in the subpleural lymphatics are exposed and vulnerable to irradiation therapy so that if it is used over an area sufficiently large to include a generous field around the visible mass the e of the les on may be narrowed down

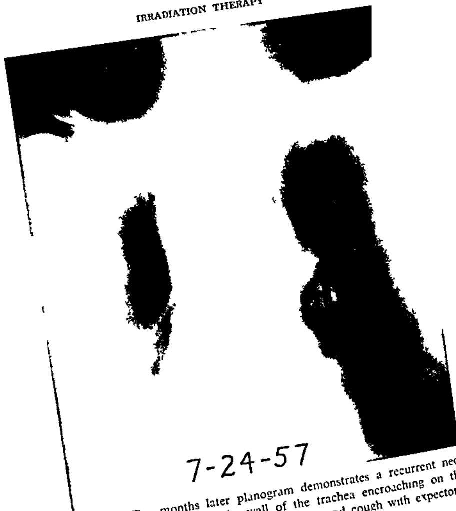


Fig 10b Ten months later planogram demonstrates a recurrent neoplasm which has invaded the wall of the trachea encroaching on the lumen The patient complained of wheezing and cough with expectoration of bloody sputum

resection offers a better chance of cure

The authors have treated two patients with peripheral bronchogenic carcinomas invading the chest wall with a combination of preliminary irradiation followed by re section Both patients had lesions in the extreme right apex of the chest causing the typical syndrome associated with superior sulcus or the so called Pancoast, tumors Resection was carried out in the first patient one month following the conclusion of irradiation therapy which was given because the lesion was deemed nonresectable He is still alive, well, and free of pain a year and a half following resection of the involved segment, ribs, intercostal structures, transverse process, and a portion of the bodi of the vertabrae en bloc (Fig 5, Chap IV A second patient treated deliberately w this combination which included an alm identical resection is well and free of over six months following surgery (Fi Chap III) Examination of the rese lesion showed that the irradiation th had reduced it to an amorphous ma fibrous tissue in which it was diffic identify the cell type of the origina plasm

The objection may be raised that treat ment of these peripheral lesions by this regimen involves giving irradiation therapy to a lesion of unknown etiology The validity



Fig 10c Seven months following irradiation therapy over the recurrent neoplasm the tracheal lumen was clear Wheezing cough and expectoration had disappeared There was evidence of irradiation fibrosis

of this objection cannot be denied However the errors of diagnosis in the clinical syndrome caused by radiographically visible peripheral pulmonary lesions of this type would be few With osteolytic destruction of involved ribs and the presence of a Horner s syndrome there is even less chance of a diagnostic error Tuberculous granulomas and occasionally a dense fibrosing pneumonitis may simulate a peripheral bronchogenic carcinoma Both of these lesions are indications for resection and no harm would result due to a preliminary course of irradiation therapy prior to resection The hardship to the patient and the hazard of disseminating the neoplasm by exploratory thoracotomy and biopsy outweigh consideration of the possible infrequent error in diagnosis

TREATMENT OF METASTASES

Pain and disabilities due to blood metastases to distant parts of the be temporarily relieved by apy Severe headache and ne due to metastases to the

equipment This factor alone justifies the choice of this type of therapy over conventional types in situations where it is applicable since the undesirable effects of irradiation in an already debilitated patient may nullify the therapeutic usefulness of the treatment

Damage to the skin and underlying tissues is a factor that limits total exposure to irradiation Irradiation therapy using high doses given by conventional techniques for treatment of bronchogenic carcinoma often produces severe painful burns of the skin Final healing of the burn leaves a deeply tanned area in which there is telangiectasia Once final healing occurs however other than the disfiguration there are no unpleasant effects Super voltage techniques are capable of delivering to the region of the neoplasm therapeutic and at times cancericidal doses without causing more than a slight increase in pigmentation of the exposed skin

Esophagitis has been the most annoying complication accompanying the use of super voltage irradiation for bronchial neoplasms The symptoms of this complication are dysphagia and a burning sensation deep in the chest The dysphagia seems to result from the atonia in the muscle of the affected segment due to irradiation damage to the musculature A true esophagitis or ulceration of the mucosa in the region exposed to the irradiation probably is responsible for the burning sensation The symptoms of this complication usually become manifest during the latter part of the course of therapy The burning sensation may be somewhat alleviated by a bland diet and the use of coating agents usually employed in the treatment of esophagitis or gastritis The dysphagia may persist for many weeks following treatment It gradually becomes less annoying with time probably due to an unconscious re education in the act of swallowing

RESULTS OF IRRADIATION THERAPY

The results of irradiation therapy for bronchogenic carcinoma can be evaluated only in regard to the aim of therapy in the individual patient Since this modality is used chiefly as a means of palliation in patients having lesions not sufficiently localized to permit resection and frequently to relieve symptoms produced by metastases it should not be judged solely by its effects on survival time The value of irradiation therapy should be judged primarily on the basis of its effectiveness in palliation of the symptoms for which its use was indicated

A total of 259 of the 1180 patients who have been under our care are known to have received irradiation therapy Forty four (40 per cent of the 133 patients seen) were treated during the past year so that it is too early to evaluate the effect of therapy upon their survival time Thirty five patients treated previously have been lost to follow up There remain 180 patients who were treated more than a year ago and whose fate is known

A comparison of survival time of the 180 patients in this series who received irradiation therapy with that of untreated patients studied by Bignall showed little variation in the two survival curves (Fig 11) Bignall analyzed the survival of 255 patients having bronchogenic carcinoma who received no treatment that would affect time of survival These patients were seen at an institution where there is an active surgical program so they represented patients who were either unsuitable for surgical therapy or refused surgery Thirty nine per cent of these patients survived one year and 14 per cent two years Bignall used the date of onset of symptoms as a startin[illegible] point in determining survival time
the patients in the authors seri[illegible]
irradiation therapy experienced
[illegible] f six months from onset

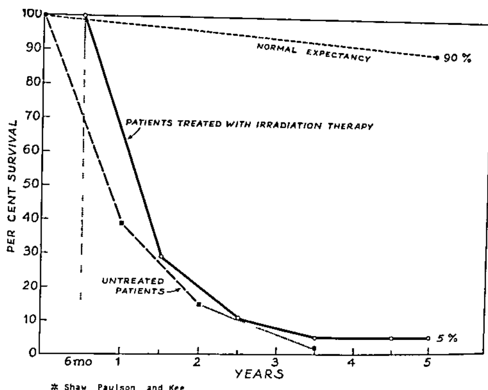


Fig 11 Bronchogenic carcinoma Survival of 180 patients treated with irradiation therapy* compared with survival of untreated patients (Bignall)

to beginning of therapy the survival curve is adjusted to start six months later than that of Bignall s patients It is granted that comparison of survival of patients comparing figures of two different groups of ob servers is not entirely valid It is surprising however, how closely the curves coincide during the first two years of observation The only significant difference in survival in these groups is the few patients who are alive and well five years following irradiation therapy Bignall observed no untreated patients surviving five years although 2 were still alive forty and forty one months following the onset of symptoms Three patients in our series of 180 patients, all with histologic proof of carcinoma, treated by means of irradiation following exploration survived more than five years One died of a cerebral hemorrhage seven years after irradiation of an epidermoid carcinoma and the other two are still alive and well eight and twelve years respectively following therapy for small cell undifferentiated carcinomas (Figs 3 and 4) Fifty two (20 per cent) survived one year, 16 (10 per cent) two years, 7 (5 per cent) three years, 5 (5 per cent) four years, and 3 (5 per cent) five years (Percentages listed are determined from the patients alive of the number eligible to survive)

Many patients who did not survive two years following therapy received relief from the distressing symptoms for which the treatment was prescribed Judged on the basis of palliation the therapy in these patients was worthwhile Shrinkage of neoplasms blocking major bronchi relieved cough and atelectasis which brought welcome respite from dyspnea The most dramatic palliation came in patients having mediastinal involvement causing tracheal and vena caval compression Many of these patients experienced relief of symptoms and enjoyed

months of trouble free productive life following irradiation and chemotherapy Control of pain by irradiation over metastases allowed others to be comfortable during their remaining months of life before return of pain again necessitated the use of narcotics The ability of irradiation therapy to modify the course of bronchogenic carcinoma indicates its use whenever localized tumor is causing disturbing symptoms

SUMMARY

Irradiation therapy occupies a major role in the treatment of bronchogenic carcinoma It suffers from the same general limitations of surgery based on the biologic factors involved in that it must be used over a lesion that is sufficiently localized to be encompassed by the therapeutic field It is not curative when used in disseminated carcinoma, but it may be useful when applied to localized lesions to relieve symptoms Irradiation is of proven value when used over local nonresectable lesions and occasionally will seemingly eradicate the neoplasm Irradiation as a preliminary treatment to resectional surgery should be considered in patients having hilar lesions that invade the major bronchi close to the carina and peripheral neoplasms that involve the chest wall The results of irradiation therapy should be judged by its ability to relieve symptoms rather than its effect on prolongation of life In a few patients, however, this modality of treatment is followed by an apparent cure of the disease

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Chemotherapy

EVERY PATIENT with a malignant bronchial neoplasm is potentially a candidate for chemotherapy. The biologic nature of bronchogenic carcinoma predetermines approximately 4 out of 10 patients suffering from this disease to be unsuitable for surgical therapy. Two out of every 10 patients will have an undifferentiated carcinoma of the round cell or oat cell type widely recognized for its rapid dissemination. Four out of 10 patients will have evidence of disseminated neoplasm at the time they first seek medical advice. Often the patient's chief complaint is due to symptoms caused by a secondary lesion rather than the primary tumor. In addition to these patients is the group of individuals who have had surgical resection that are subsequently discovered to have disseminated neoplasm who may become candidates for chemotherapy. If chemotherapeutic agents can destroy neoplastic cells free in the blood stream it may be useful when given at the time of or immediately following resection of localized neoplasms to prevent dissemination. Thus, chemotherapy alone or combined with surgery or irradiation therapy, plays a role in preventing dissemination, delaying the growth of the neoplasm, increasing survival time, and in allaying distressing symptoms.

What do we have to offer patients with disseminated neoplasm? Irradiation therapy which is considered in another chapter will be of great benefit to many of these patients. But irradiation therapy like surgery must be able to narrow its effect to a local region. Like surgery it can offer little of value in disseminated cancer except to relieve temporarily pain or control cough. Control of a disseminated neoplasm can only be accomplished by some agent that can pass through the blood stream to every part of the body. This agent must be selectively injurious to the malignant cell in doses that can be tolerated by the normal tissue cells.

AVAILABLE CHEMOTHERAPEUTIC AGENTS

Cancer tissues and normal tissues have similar biochemical components, but enzymatic function is less in neoplastic tissue. Low metabolite activities in malignant cells make them vulnerable to appropriate antagonistic chemotherapeutic agents of the antimetabolite group. Shapiro has demonstrated that as the enzyme concentration in a tissue becomes lower, the degree of inhibition by the antagonist of the enzyme becomes greater. This investigator also found some chemical agents used alone to be capable of producing only carcinostasis. Kligerman and Shapiro have published evidence of the efficacy of chemical agents in sensitizing the tumor cells to irradiation therapy in carcinoma of the breast in experimental animals.

As in the case of radiotherapy, tumor doses of chemicals must be compromised because of injury to normal tissues by carcinocidal doses. Repeated or prolonged administration of excessive doses of chemotherapeutic agents alone or combined with irradiation therapy may result in cumulative toxic effects to the normal cell as well as the neoplasm. The risk of depression of

the hematopoietic system (bone marrow) is particularly great, resulting in severe primary anemia, leucopenia, and thrombocytopenia This risk must be calculated and should be explained to the individual patient and his family prior to the institution of such therapy

MECHLORETHAMINE HYDROCHLORIDE AND RELATED DRUGS

Mechlorethamine hydrochloride is the only nitrogen mustard compound that has been released for general use by the medical profession The authors' experience has been largely limited to the use of this drug Triethylene melamin (TEM) which is a compound that can be administered orally has been released for experimental use Our experience with this drug has been more limited but in general it seems to produce about the same response as nitrogen mustard given intravenously Our observations on the effectiveness of triethylene thiophosphoramide (Thiotepa) have been too limited to warrant a comparison with nitrogen mustard It seems to be less toxic and to give fewer unpleasant symptoms during administration The difficulty in evaluating response to these drugs because of the vagaries of the disease being treated and the lack of controls make it almost impossible to compare their therapeutic effectiveness

DOSAGE AND METHOD OF ADMINISTRATION

In our use of the nitrogen mustard compounds we have varied the dosage and the method of administration from time to time Early, impressed by the toxicity of the drug the usual adult patient was given eight to ten milligrams in four divided doses in as many days Later, influenced by the reports of other workers, we became bolder and gave in a single dose 0 5 mg per kilogram of body weight, making the total dose for the average patient 35 to 40 mg This dose seemed to be well tolerated although transient nausea and vomiting and phlebo thrombosis of the vein in the arm used for the injection occurred in almost every patient Our present plan of administration is to give a total dose of 0 5 mg per kilogram of body weight in four divided doses on consecutive days The treatment is given following the evening meal so that the patient has the night to recover from the nausea and vomiting that almost uniformly follows the injection The injection is given by starting an intravenous drip of 1000 cc of 5 per cent glucose in distilled water to which 50 mg of chlorpromazine has been added to counteract the nausea When it is certain that the needle is in the lumen of the vein, the tubing is clamped close to the adapter The nitrogen mustard compound dissolved in 10 cc of distilled water is then injected into the tube taking about ten seconds to make the injection The clamp is then released from the tube and the intravenous drip allowed to continue

TEM which is administered orally is supplied in five milligram tablets The usual course of treatment we have employed is a total dose of 25 mg giving one tablet on each of five successive mornings on an empty stomach one hour before breakfast This therapy can be taken by the patient in the home He should, however, be under close observation by his physician due to the danger of the toxicity of the drug to the bone marrow Repeated courses of therapy have been given at six to twelve week intervals The risk of depression of the bone marrow makes imperative blood counts before and at weekly intervals after the administration of any of the nitrogen mustard drugs

OBJECTIVE EVIDENCE OF VALUE

Since chemotherapy is not capable of curing neoplasms of the bronchi, wha jective evidence is there that it is

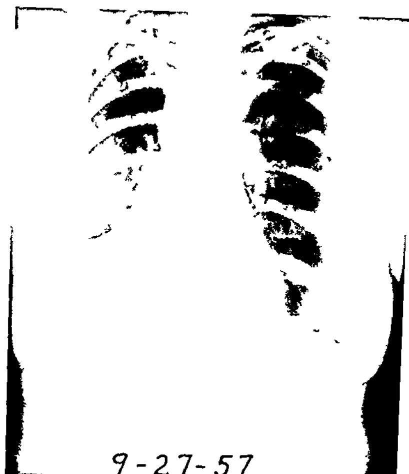


Fig 1a This 50 year old woman was found on examination of a cervical node to have a small round cell undifferentiated carcinoma that had caused cough dyspnea and substernal pain She was treated with irradiation therapy and experienced temporary relief of symptoms

therapeutically? Karnofsky *et al* reported a most careful detailed study of the therapeutic effects of nitrogen mustard therapy in 25 patients with proven bronchogenic carcinoma found to be inoperable Seventy four per cent of these patients improved symptomatically and 49 per cent had objective evidence of improvement Skinner Carr and Denman[4] reported palliation of symptoms with nitrogen mustard therapy but found no evidence that life was prolonged Lynch *et al* treated 60 inoperable patients with nitrogen mustard as the only therapy They found that more than half showed objective evidence of improvement with the greatest percentage being in the patients having undifferentiated neoplasm The favorable response was at times brief in duration but they felt the therapy had definite value in the inoperable patient

Several observations can be set forth testifying that the benefit is real and not imaginary Patients having severe headaches due to brain metastases may experience gratifying relief for a period of time following nitrogen mustard therapy The severe lancinating pain caused by spinal metastases often is greatly relieved so that life becomes more tolerable Swelling of the neck shoulder, and arms due to vena caval compression by mediastinal nodes will frequently dramatically disappear following a

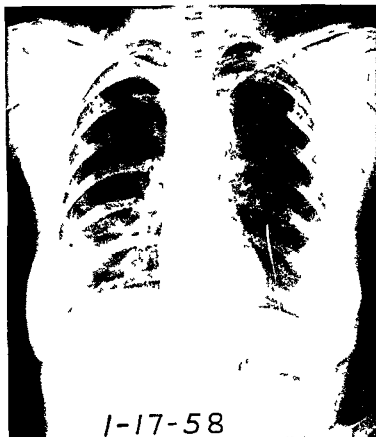


Fig 1b Less than four months later the atelectasis of the lower and middle lobes had cleared She was admitted to the hosp tal because of extreme fatigue and left hemianopsia Her liver was found to be enlarged and nodular Sixty mill grams of nitrogen mustard was given intra venously in six d vided doses over a period of two weeks

course of chemotherapy Palpable cervical nodes can be observed to reduce in size fol lowing this therapy Frequently a patient incapacitated by severe lassitude when given a course of therapy will experience a feeling of well being and again renew pursuits in which he had lost interest (Fig 1) It is true that these benefits are quite transitory being carcinostatic rather than carcinocidal but they are real and are appreciated by the patient and the family The availability of this therapy should not be overlooked so that the patient in discouragement seeks help outside of the medical profession from cancer quacks

COMBINED WITH IRRADIATION

Biochemical means either to sensitize the tumor cell to or augment the effect of irradi ation therapy by a cancerostatic effect is de sirable and should be explored further clini cally It is true that with combined therapy it is difficult to assess results of treatment However in dealing with a fatal disease all modalities of therapy that may be of value should be utilized Irradiation can only be used effectively when focused on a limited region of involvement such as the primar tumor mediastinal masses and and spinal metastases If evidence dissemination of the carcinoma

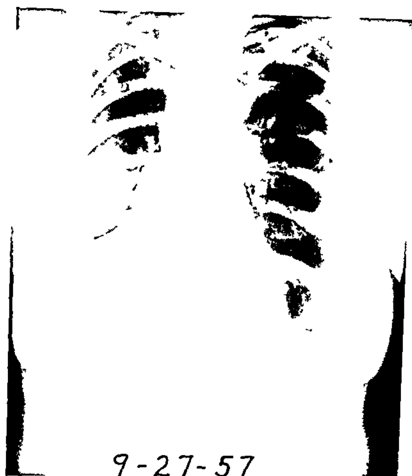


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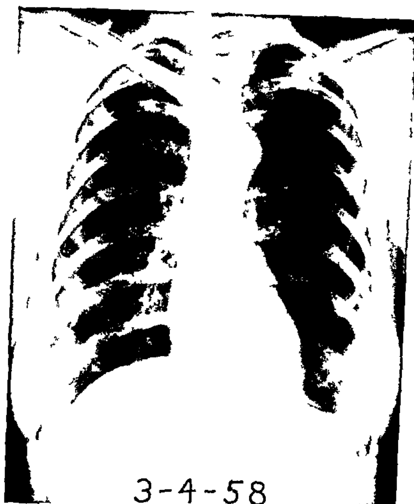


Fig 1c Eight weeks following initiation of chemotherapy the chest appeared normal palpable nodes in the neck had disappeared vision was normal and the patient had returned to work completely symptom free

can be used to control the more obvious or symptom producing lesions and chemotherapy be given for the disseminated lesions Where irradiation has been used as *initial therapy* and cannot be repeated chemotherapy may be used later when there is evidence of relapse or dissemination

COMBINED WITH SURGERY

The value of the use of chemotherapy given at the time of or immediately following *pulmonary resection for bronchogenic* carcinoma is not yet proven From both clinical and animal research there is evidence that it should aid in the control of dissemination of the neoplasm Engel[8] has been able to demonstrate neoplastic cells in the blood aspirated from veins draining neoplasms of the colon stomach and kidneys at the time of surgical resection of these lesions in 54 per cent of cases *Fisher* and Turnbull[7] found tumor cells in the venous blood in 32 per cent of 25 specimens of colorectal carcinoma examined by them Moore Sandberg and Schuberg[8] identified neoplastic cells in the venous blood in 93 out of 179 cases (52 per cent) of visceral carcinoma studied by them They recovered tumor cells in the blood in 60 out of 109 (55 per cent) patients at the time of surgery This indicated to them that sur

gery might be an important factor in dissemination of carcinoma cells. These findings have been confirmed by Cole and his co-workers.[9,10] Cole further demonstrated that in experimental animals nitrogen mustard injected into the blood stream has prevented implantation of neoplastic cells introduced by intravenous injection of a free suspension of these cells. If this is also true in the human patient, nitrogen mustard given intravenously at the time of surgery could prevent survival and implantation of malignant cells that might be freed into the blood stream by handling of the lesion at the time of surgery. That dissemination of the disease at the time of surgery is a hazard should be recognized by every surgeon. Recent reports in the literature emphasize the importance of blood vessel invasion by the neoplasm as a major factor in the prognosis for long term survival (Collier *et al.*[11]). Chemotherapy may be helpful in modifying the hazard of this pathologic aspect of the disease.

It would seem reasonable to give nitrogen mustard in an intravenous drip at the time of surgery or in the immediate postoperative period in every patient having a resection or exploratory thoracotomy for bronchogenic carcinoma. The authors have recently used chemotherapy as an adjunct to surgery in a few patients. The series of patients thus treated is too small and the time elapsed since surgery too short to allow evaluation of this combined therapy. The risk of bone marrow depression in the postoperative patient may outweigh the benefits, however.

CHEMOTHERAPY FOLLOWING EXPLORATORY THORACOTOMY

The surgical mortality and poor survival time following exploratory thoracotomy for bronchogenic carcinoma when the lesion is found to be non-resectable has already been discussed in previous chapters. Chemotherapy probably could not modify the surgical mortality but conceivably it could favorably influence a longer survival time by preventing the implantation of cells set free in the blood stream by the trauma of surgery and retarding the development of metastatic lesions already present. Following thoracotomy the patient must necessarily be hospitalized for a period of time. This time can well be spent in the giving of a course of chemotherapy. The addition of chemotherapy during the period when narcotics for relief of pain and intravenous fluids are being used adds little to the discomfort of the postoperative course of the patient. In addition to the actual therapeutic benefit there is the value of the increased morale of the patient and the family in knowing that something is being done to combat the disease. However, the increased risk of bone marrow depression in combined therapeutic and irradiation programs must be considered.

CHEMOTHERAPY FOR MALIGNANT PLEURAL EFFUSION

Pleural effusion due to extension of the neoplasm to the pleural surfaces is a frequent complication of bronchogenic carcinoma. It is typically painless but usually it causes dyspnea. For a time the dyspnea can be controlled by frequent thoracenteses. These repeated aspirations of the pleural fluid are disturbing to the patient and any therapy that can stop the formation of the fluid is helpful in the management of the case.

Solutions of radioactive gold and phosphorus have both been used intrapleurally to help control pleural effusion due to neoplasm. Although both of these agents have been of proven value the cost of production, the short half life (making transportation and arranging for administration difficult) and the technical precautions that must be observed in the handling of these agents makes their general application impractical. Nitrogen mustard or Thiotepa given intrapleurally seemingly have about the same

beneficial effects as the radioactive substances and have the advantage of being less expensive, easier to handle, and more readily available When used intrapleurally approximately the same dose can be used as is given with a course of intravenous therapy, 0 4 mg per kilogram of body weight The same precautions should be used in watching for damage to the bone marrow following the use of chemotherapy intrapleurally as intravenously Intrapleural injection of nitrogen mustard can be repeated at shorter intervals (two to four weeks) if the pleural fluid is still forming and no anemia has resulted from the initial injection

COMPLICATIONS OF CHEMOTHERAPY

The immediate complications of nitrogen mustard therapy when given intravenously are nausea and vomiting and phlebothrombosis of the vein used for the injection The nausea and vomiting can be minimized by giving the therapy following the evening meal so that the patient has a long period of induced sedation before the next meal Fifty milligrams of chlorpromazine can be given in the intravenous drip that follows the injection of the nitrogen mustard compound This can be supplemented by 25 mg doses of chlorpromazine by mouth or intramuscularly at intervals as indicated by the individual reaction of the patient

The complicating phlebothrombosis although annoying is not a serious problem Usually no therapy is required other than assurance to the patient and family that the condition will clear with time Elevation of ... t heat may ... Although ... in several patients in none was it a serious factor in the management of the overall problem

The most serious complication of nitrogen mustard therapy is due to its depressing effect on the hematopoietic system A profound thrombocytopenia, leucopenia, and primary anemia may result This complication usually becomes apparent two weeks following therapy It follows both the use of nitrogen mustard intravenously and TEM orally It is more likely to occur following repetition of therapy

The blood of the patient who has received chemotherapy should be studied once a week following therapy This study should include a platelet count as well as a count of the cells The most serious aspect of depression of the bone marrow is damage to the megakaryocytes leading to thrombocytopenia The finding of a low platelet count can be checked with a study of the sternal bone marrow The reason that thrombocytopenia is so serious is that as yet there is no effective treatment for it The use of transfusions of fresh blood and steroid therapy may be of help but there is no assurance that the condition can be controlled Death may occur quickly due to generalized capillary bleeding

The patient can usually be supported during a period of agranulocytosis by blood transfusions and penicillin therapy Folic acid in adequate dosage may also be of value while the white count is low

The primary anemia is usually of less concern since citrated blood can be given in adequate amounts as replacement therapy until the period of bone marrow depression has passed

Two patients that we have treated with nitrogen mustard therapy have died due to uncontrolled thrombocytopenic purpura In both instances therapy had been repeated after an initial favorable response in treating disseminated carcinoma Admittedly the risk of nitrogen mustard therapy is real and death may result but in treating such a serious condition as disseminated carcinoma risks must be accepted Surgeons are prone to make little of the risks of surgical therapy and shrink from the risks of medications Internists in contradistinction emphasize ... s but are complacent

about severe complications of drug therapy Both groups must realize that to take an aggressive attitude toward the treatment of malignancies implies the calculating and incurrence of risk of complications

REPETITION OF CHEMOTHERAPY

Chemotherapy can be repeated The decision as to whether it should be repeated would depend upon (1) a favorable response to the initial course (2) the absence of evidence of depressed hematopoiesis and (3) an appraisal of the general condition of the patient Usually at least six to twelve weeks should elapse between courses of therapy to allow time for observation of a favorable response and to check damage to the hematopoietic system It would be unwise to repeat nitrogen mustard therapy in a patient rapidly approaching a terminal state The dosage employed in subsequent courses is generally the same as that used in the initial treatment Oral TEM administration may be employed as a subsequent course of therapy following the initial intravenous nitrogen mustard treatment

CONCLUSION

Chemotherapy now available constitutes an important means of treatment of the majority of patients suffering from bronchogenic carcinoma At the present time chemotherapeutic agents appear to be capable of producing carcinostasis only through inhibition of enzymatic function of neoplastic tissue The beneficial results can best be evaluated in the relief of distressing symptoms and the causing of a sense of well being rather than in a lengthening of the survival time If a patient can be kept reasonably comfortable and maintain an interest in life during the greater part of the terminal illness something useful has been accomplished It is in this realm that chemotherapy is of value The ultimate hope of cancer research is that in time a substance will be found that will be carcinocidal either by selectively destroying the cancer cell or by depriving it of some chemical substance necessary for its survival In the meantime induction of quiescence by means of chemotherapeutic agents alone or in combination with irradiation therapy warrants further exploration

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Terminal Care

CARE OF THE PATIENT having a bronchogenic carcinoma who cannot be cured by surgery is undoubtedly the most important, yet at the same time, the most difficult and neglected phase of the management of this disease. Less than one third of the patients may have surgical excision of the neoplasm, and only a small percentage of these can be regarded as cured. Another one percent may receive an apparent cure from irradiation and chemotherapy. The remainder unless death results from some other cause eventually succumb to the effects of the cancer of the lung. For some the course of the disease may be rapid with death ensuing within a few weeks of the detection of the disease. Many of the incurable patients will live more than a year from the time of diagnosis and a few will survive for several years. It is the responsibility of the physicians caring for these patients to make this period of survival as comfortable and as productive as possible.

As a profession in our evaluation of the results of the treatment of any particular disease there is a tendency to place too much emphasis on "cure" and the "saving of lives." In the last analysis we do not save lives. We merely prolong lives. If a patient under treatment experiences months and even years of reasonably comfortable happy productive living, no credit is given to the medical management. His death is listed in vital statistics as due to a certain disease and the treatment is considered as having failed. Prolongation of life and relief of suffering are difficult to evaluate statistically and objectively. Nevertheless, this function is the major one confronting the physician caring for a patient having a disease that cannot be cured.

The majority of people accept the fact of ultimate death although if one is living a satisfactory life and is in full command of his mental and physical faculties, the desire to stay alive as long as possible is ever present. It is a severe shock to the average patient to come face to face with the realization that he is suffering from an incurable disease. Many do not want to know or if informed of the diagnosis, and its implications are explained to them, in a natural human reaction to escape harsh reality, rarely completely realize what is happening to them. Even if one accepts the fatal implications of the condition from which he suffers he can maintain good morale provided hope is not destroyed, the date of death is uncertain, and distressing symptoms can be somewhat alleviated. A patient should never be told there is nothing more that can be done for him and a date for death prophesied. The result too often is complete dissolution of morale, destruction of hope, and panicked search for benefits from quasi therapeutists of cancer. It is fair to give the patient some insight as to the problem he faces but the physician must re-enforce hope through assurance that he will stay with him and do all in his power in the coming struggle for survival.

WHAT SHALL THE PATIENT BE TOLD?

the problem arises "w

the patient be told?" There is no easy answer to this question There are too many variables involved The physician must consider the probable extent of the neoplasm It is usually best to talk to the patient referring to the lesion as a *tumor* If this satisfies the patient and the lesion is one that surgery may cure, no other term need be used If, however, when confronted with a patient whose lesion is probably curable, one senses that surgical recommendation will not be readily accepted, it may be necessary bluntly to inform the patient that he has a cancer Otherwise, the patient has no true basis of fact other than his confidence in his doctors on which to base such an important decision as to whether or not he should accept surgery Unless pathologic proof of the nature of the lesion has been obtained, the physician or surgeon is not justified in talking positively of the lesion as being a cancer or a malignant one Errors in clinical diagnosis are possible in even what appears to be a clear-cut situation Such an error may cause irreparable damage to the morale of the patient even though he is assured later that he did not have a malignant lesion As a corollary of such an erroneous clinical diagnosis are the medico legal implications and at least the unfavorable reflection on the physician's ability

The more difficult problem arises when the diagnosis of cancer of the lung has been proven or is clinically obvious in a patient whose lesion is incurable by surgery If possible, the diagnosis and the position in which it places the patient should be discussed with the patient's family, especially the husband or wife The physician should generally be guided by the wishes of the spouse as to what the patient should be told Many married couples have a pact that they will not deceive each other about such important matters and their wishes should be respected Evading the question of the true diagnosis *in such a situation results* in loss of confidence in the physician since the patient s spouse will inform him At the request of the family, or if confronted with a direct question that permits no evasion, the true diagnosis and the outlook for survival *should be disclosed* to the patient This disclosure need not be abrupt and should be made with all compassion and hope The blow to the patient's morale can be softened by intimating that treatment is available to delay the malignant process and to alleviate the more unpleasant symptoms

THE FAMILY'S ROLE

The major task in the care of the patient will usually fall upon the family It is necessary, therefore, that they be fully informed concerning certain aspects of the disease some of which the physician may not wish to disclose to the patient They *must be instructed* to encourage the patient to maintain activity in any pursuits he enjoys that are within his physical capacity As long as the patient is ambulatory and reasonably comfortable work visits to relatives, fishing trips and even tours abroad should be encouraged All such activities if genuinely desired and enjoyed by the patient will not only fill his remaining days with interest, but will probably actually prolong his life There is no point in urging such activities if the patient's condition has deteriorated to the point that the capacity to enjoy life has vanished

Preservation of morale may depend a great deal upon the patient s appraisal of his usefulness to his family Return to work after initial treatment is *desirable even* if the estimated time of survival may be *short* Housewives and mothers should be encouraged to take up their usual *responsibilities* in the home, even though *the limitations* imposed by their disease may make it necessary for others to *share in the* household duties Every effort should be made to prevent invalidism being *imposed* by over

solicitous relatives or being prematurely accepted by the patient because he has lost hope

THE ROLE OF THE FAMILY PHYSICIAN

The family physician often bears the brunt of the professional care The care of the incurable patient is seldom pleasant and sorely tests the faculty of the art of medicine Numerous and repetitious questions must be patiently answered, always keeping in mind "how will he interpret this answer?" Often drugs must be prescribed with full realization that they cannot possibly correct the condition or completely relieve the symptoms for which they are prescribed Details concerning diet, rest at night, and habits must be discussed Problems troubling the patient no matter how trivial must be resolved to the best of the doctor's ability The physician and the religious counsellor will share in the support of the morale of the family as well as that of the patient

THE ROLE OF THE CONSULTING SURGEON

The role of the consulting surgeon may be brief in point of time and few in the number of contacts with the patient but nonetheless is very important by virtue of his experience As far as the patient is concerned the consulting surgeon is the court of last appeal He is the one who has interpreted the roentgenograms, seen the tumor through the bronchoscope, or opened and explored his chest He has determined the course of treatment to be followed It is only natural that the patient should look to the consulting surgeon for counsel and later in his care should refer major problems back to him for solution Even though the surgeon cannot cure the patient by resection of the neoplasm, his responsibility to the patient remains

It is the duty of the consulting surgeon to discuss the diagnosis and prognosis with the patient and family even though in the patient's interest he may not tell the entire truth Working with the referring physician, he should arrange for irradiation therapy if such seems indicated He must make recommendations for and at times carry out himself indicated chemotherapy The referring physician must be fully informed as to the diagnosis, prognosis, and general plan of future care Likewise, he must be told what information has been given to the patient and the family so that he will not inadvertently divulge facts that may have been withheld

Unless distance is a barrier, the consulting surgeon should see the patient periodically for checkup examinations These examinations can mean much to the support of the family and referring physician in their care of the patient even though therapeutically little seems to be accomplished It means much to the patient to be examined Every finding should be presented in its most favorable light Drug schedules may have to be rearranged, some discarded if they seem ineffective, and new ones prescribed Any new development in the field of cancer therapy of which the patient has become aware should be discussed with the patient The new therapy, if ethical, should be tried in applicable situations, or the fact that the treatment is not suitable should be explained to the patient's satisfaction The patient should gain the impression that everything possible is being done to combat his disease When making the appointment for the next visit, a definite time should be set in the future so that the patient gains the impression that the consulting surgeon confidently expects him to be able to return at that future date

TREATMENT OF SYMPTOMS

Specific measures in the treatment of the incurable patient are related to the reli of cough dyspnea, pain, hemorrhage

general debility Vena caval and tracheal obstruction cause most unpleasant symptoms The treatment for relief of these two complications of bronchogenic carcinoma are discussed in the chapters dealing with irradiation and chemotherapy

COUGH

Cough is a frequent symptom that may represent the major problem disturbing the comfort of the patient Although some cough may have been present for years as a "smoker's cough," the increasing persistence of the cough and the severe paroxysms of it may become intolerable The physical exertion demanded in coughing and the disturbance of rest may be a major factor in the deterioration of the patient's physical condition

Cough may be caused by the obstruction of the bronchi or trachea by neoplasm, pressure on the trachea or bronchi, or by an associated bronchitis Irradiation therapy and chemotherapy may give temporary relief of the cough by causing regression of the neoplasm Bronchoscopy with manual removal of neoplastic tissue may open the airway for a period of time Repeated bronchoscopies for this purpose are rarely justified In selected patients palliative resections may be justified for the sole purpose of eliminating the causes of harassing coughs Vagotomy below the branching of the recurrent laryngeal nerve has been advocated as a useful measure to relieve cough in patients found to be non resectable at the time of exploration Daily administration of low doses of antibiotic drugs combined with expectorant cough medicines will be of value especially when the cough is due to bronchitis Attempts to control a cough due principally to bronchitis will be futile if the patient persists in smoking cigarettes excessively As a general principle it is not kind to quarrel about a lifelong habit with a patient whose life expectancy is short If cough is a major distressing symptom and it is seemingly due to bronchitis the importance of eliminating bronchial irritation by refraining from smoking should be ex plained to the patient

The administration of antitussive agents and narcotics eventually becomes the main measure required to control the severe cough Codeine and hycodan may be used initially in effective doses The doses may have to be increased as time passes When these drugs are finally ineffective, dilaudid should be used It is the most effective available narcotic for the control of cough It can be added to any vehicle in strength so that each dose will give 1/64 gr At this level of dosage, given three to four times daily, even a severe cough can be almost eliminated

DYSPNEA

Dyspnea may be due to loss of the airway to a lobe or an entire lung by the obstructing neoplasm or compression of the lung by pleural fluid More often dyspnea is due to an associated generalized pulmonary emphysema resulting from chronic obstructive bronchitis A failing heart due to the mounting pressure in the pulmonary arter may contribute to dyspnea in the termi state

Relief of the bronchial obstruction te porarily may result from manual removal bits of neoplastic tissue through the bro choscope Irradiation therapy over the o structing neoplasm may cause absorptic of the tumor and allow the bronchus reopen resulting in dramatic relief of dy pnea cough and pain

Accumulations of pleural fluid should b removed by thoracenteses as often as re quired to relieve the patient's dyspne Nitrogen mustard derivatives and radioiso topes introduced into the pleural cavity ma delay and even stop the formation of fluid Irradiation therapy has a definite role in th treatment of pleural fluid formation due to neoplastic invasion of the pleura As th

neoplastic infiltration of the pleura progresses the time is reached when no more fluid can be aspirated and the resultant loss of pulmonary function leaves the patient with dyspnea which cannot be relieved At this point sedation and narcotics should not be withheld even though in general they are contraindicated in the severely dyspneic patient

Dyspnea due to an associated pulmonary emphysema can often be partially relieved by a vigorous attack on the generalized bronchitis Expectorant cough mixtures and bronchodilating drugs should be prescribed for daily use Often an element of infection is present that can be partially eliminated by the use of antimicrobial drugs using a low daily dose Positive pressure breathing techniques using wetting agents may help improve ventilation This therapy can be instituted in the hospital and if the prognosis from the standpoint of time makes it advisable the equipment can be obtained by the patient and used in his home

Tracheostomy is useful in the relief of dyspnea in the emphysematous patient It finds its greatest usefulness immediately following resection in the patient with borderline pulmonary function Its use in the incurable patient suffering from severe dyspnea as a measure of prolonging life for a short period does not seem justified

PAIN

Pain is always a difficult symptom to control Bronchogenic carcinoma in the periphery of the lung may invade the pleura causing a severe localized pain at the site of the lesion Further extension into the ribs and intercostal nerves will result in severe unrelenting radiating pain along the nerve distribution The most severe pain is caused by the invasion of the nerve routes making up the brachial plexus by a peripheral carcinoma in the superior sulcus of the chest the so called Pancoast tumor" Bronchogenic carcinoma commonly metastasizes to the spine invading the vertebrae and at times the neural canal The involvement of the nerve roots either due to direct invasion or impingement at the interneural canal results in severe pain of the radicular type Invasion of the sympathetic chain causes an intense poorly localized burning type of pain within the chest

Palliative resections may be very useful to control pain when a peripheral neoplasm in the lung has invaded the chest wall Irradiation therapy is usually not successful in relieving pain due to direct extension of a neoplasm into the parietes of the chest It does however yield gratifying relief when used to control pain due to spinal and bony metastases Headaches due to cerebral metastases are frequently temporarily relieved by irradiation therapy over the site of the secondary lesion Chemotherapy often gives gratifying results in helping to relieve pain due to both the primary and secondary lesions Nerve blocks in certain instances of localized parietal pain have been effective

Neurosurgical procedures for the relief of pain have a definite place in the treatment of these patients Cordotomy and intercostal neurectomy may relieve the pain due to lesions below the mid thoracic level They will be of no help to the patient with brachial plexus involvement Intramedullary spinothalamic tractotomy has been observed to give complete relief of pain in this type of neural involvement and should be considered if it is felt that the patient's estimated survival time is at least six months This surgical procedure has the disadvantage of carrying considerable risk and of being a technique which has been mastered by few neurosurgeons Return of severe pain following intramedullary tractotomy is usually due to further extension of the neoplasm to nerve pathways beyond the limits rendered insensible by the procedure D Errico has described the

limitations complications and technique of this neurosurgical procedure

HEMOPTYSIS

The coughing up of blood is alarming to a patient The typical bleeding from an obstructing carcinoma in the bronchus is an oozing of blood which is expectorated mixed with mucus Irradiation therapy may be successful in eliminating this distressing sign In selected cases where the bleeding is severe, palliative resection is useful Drugs generally used to improve the clotting mechanism or to reduce capillary fragility are of little practical value in coping with bleeding from bronchial neoplasms At times their use is justified for psychologic reasons to help the patient realize that everything is being done for him In the face of severe life threatening hemorrhages from the bronchi in the incurable patient heavy sedation and the liberal use of narcotics is not only justified but mandatory to allay the patient s apprehension even though their use may hasten death

GENERAL DEBILITY

Weakness or general debility may be the main complaint and at times the only complaint of the patient suffering from a disseminated carcinoma This is the usual complaint if there has been destruction of the adrenal glands by metastases In this situation the use of steroids as replacement therapy may be of temporary value High potency vitamin and protein preparations seem to be of value in some of these patients. Marsilid and Isoniazid given in doses of 300 mg daily have a stimulating effect and may for a period help to increase the appetite The tranquilizing drugs also have their place in the treatment of these patient by counteracting some of the mental depression that inevitably accompanies the realization that he is afflicted with an incurable disease

THE REWARDS OF TERMINAL CARE

Some of the closest human relationships between a physician and his patient develop during the care of the incurable patient The patient and the family are eternally grateful for the attention and consideration shown them by the physician during this trying period Words of cheer and consolation patient attention to the patient s complaints readiness to make available any drugs that may be required and a firm handshake at the end of a period of consultation can all do much to lighten misery during the days of terminal illness

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Results

EVALUATION OF RESULTS of therapy for cancer of the lung is a complex problem To demonstrate that therapy has had a beneficial effect on the time of survival it must be shown that the survival curve departs from the survival curve of untreated patients having the same type of disease and approaches the survival curve of people of the same age and sex who do not have cancer of the lung Although the survival curve of healthy people is well established the curve of untreated patients having bronchogenic carcinoma is often impossible to establish because of the difficulty in establishing the time of onset of the disease To diagnose a cancer earlier in its course is to increase survival time by a similar period even without treatment The ability accurately to assess the quality of survival is even more confusing In order to arrive at a reasonable prognosis in the case of a particular patient being considered it is necessary to know the clinical course of neoplasms of a similar type This means that in addition to the determination of the overall survival rates of patients it is necessary to determine survival rates according to the special categories in the broad picture of bronchogenic carcinoma

Reports in the literature dealing with survival and cure following surgical excision of bronchogenic carcinoma are confusing due to the variety of methods of reporting used by various authors Percentages are stated but there is a great variation in what is considered the base line Some authors include only carcinomas histologically proven This ignores a significant group of patients in whom an accurate clinical diagnosis can be made but it is either not feasible or unwise to obtain histologic proof Patients having cerebral metastases gross mediastinal involvement with vena caval or tracheal compression spinal metastases superior sulcus tumors paralyzed vocal cords fluid due to pulmonary venous occlusion severe pulmonary emphysema and advanced age all may fall in this group It is true that an occasional error may be made in making a clinical diagnosis of primary cancer of the lung not supported by histologic confirmation but in any large series of patients followed for a significant period of time the percentage of error would be small Unless these clinically diagnosed patients are included in the total evaluation the fate of approximately one third of patients having cancer of the lung will be ignored and the statistics will be weighted in fa or of the surgical cases Reports from various clinics reporting on total experience reveal that histologic proof is obtained in approximately 70 per cent of the patients having cancer of the lung This percentage remains remarkably stationary but may vary with the attitude of the physicians as to what lengths are justified to obtain tissue confirmation

OPERABILITY AND RESECTABILITY

Operable patients are those [illegible] ha[illegible]ns that can be removed o[illegible]t may benefit by

section At the time thoracotomy is performed, a certain *percentage of operable* patients will be found to have lesions that can be removed and are then designated as being *resectable* Conversely, a particular lesion may be resectable but *inoperable because of distant metastases or cell type* Thus, resectability is not synonymous with operability Operability and resectability rates will reflect the attitude of the surgeon's aggressiveness in applying surgical therapy *An excessively high operability rate in relation* to the resectability rate indicates an unjustified tendency to perform exploratory thoracotomy for all lesions regardless of the possibilities of resection and the inherent *mortality rate for thoracotomy for the non* resectable carcinoma A policy which is too aggressive as far as resection is concerned will be reflected in a high operative mortality and in a smaller percentage of patients surviving the first year *following operation* The percentage of operable and resectable cases will appear high if only histologically proven cases are used as the base line of 100 per cent excluding the cases diagnosed *by clinical means alone Ideally, in order* to limit induced surgical morbidity and mortality as much as possible, the operability rate should not be excessively greater than that of resectability Every effort should *be made to establish the resectability of a* lesion before thoracotomy is performed This does not preclude the necessity of exploration in doubtful cases in order to establish the correct diagnosis

REPORTING OF RESULTS

Reporting of survival following resection also varies with authors Some report percentage of survival of all cases resected while others report survival of *those* recovering from the resection This latter method is not objectionable as long as the total number of resections and the operative mortality are clearly stated

Composite *results of surgical therapy* would be easier to compile if a uniform *method of reporting became standard* The most logical method would seem to be one in which 100 per cent included as a base line all patients seen with cancer of the lung, including both clinically diagnosed *and histologically* proven cases The operability rate would then be the percentage of this total group thought to be suitable for surgical therapy Likewise, the resectability rate would refer to that proportion of the total group in whom resection was performed It is of benefit to divide this group into resections thought to be curative and those considered palliative provided the classification is made at the time of surgery *The surgical mortality should include* all patients dying within a month of surgery whether or not they died in the hospital It should also include later deaths due to complications directly relating to the surgery *Survival rates are pertinent for* the separate groups receiving surgical therapy irradiation, and chemotherapy as well as the salvage rate of the entire group Such uniform reporting would place the evaluation *of therapy in proper perspective* and should lead to an improved rationale of therapy

REPORTS OF OTHER AUTHORS

Husfeldt[1] has reported the total experience with surgical treatment of bronchogenic carcinoma in Denmark In the year 1949 50, 450 cases of cancer of the lung were detected Ninety three patients (21 per cent) underwent total pneumonectomy Seventy nine patients *survived the operation* and of these, 24 were alive and well five years later This represents a 5 per cent salvage of the entire group These results are significant since they are reported from *a country with a uniform* population cared for by a well organized medical system with care available to all The total cases reported probably represent *as all inclusive* a base from which to evaluate the results as it is possible to obtain

Latourette, Lampe, and Hodges[3] reported the total experience of the University Hospital at the University of Michigan with survival in bronchogenic carcinoma Up to 1954 1,207 patients had been seen Five and two tenths per cent of the 591 patients eligible had survived five years This report is from the 'Organized Medical Investigation of Cancer" being carried out at this institution and thus represents an unselected group of patients Seventy-two per cent or 867 patients of the total series had positive histologic proof of primary carcinoma of the lung

Churchill *et al* [4] in 1950, reported the experience at the Massachusetts General Hospital with 1,130 patients in which a clinical diagnosis of carcinoma of the lung had been made Sixty per cent (681) of these had histologic proof of diagnosis Out of this entire group 26 per cent (294) were subjected to thoracotomy and 15 per cent (171) were resected Of the resected group 114 underwent pneumonectomy and 57 lobectomy, and 137 patients survived resection The operative mortality for pneumonectomy was 22 8 per cent and for lobectomy 14 per cent The mortality for patients operated upon during the last two years covered by the report was 3 7 per cent for pneumonectomy and 3 8 per cent for lobectomy — a truly praiseworthy record Of the 48 patients who had pneumonectomies more than five years before reporting 6 (12 per cent) were alive Similarly, of the 21 lobectomy patients 4 (19 per cent) survived five years Percentage survival of the total group eligible to survive five years was not reported From the available statistics reported it appears that less than a 5 per cent salvage was achieved It was noteworthy in this report that the survival curve for patients treated for pneumonectomy practically coincided with the curve of the lobectomy group

Churchill *et al* [5] in a recent report have brought their study of the treatment of bronchogenic carcinoma up to date Between 1950 and 1957, 604 additional patients with histologically proven carcinomas have been seen Since in the previous report cases histologically proven represented 60 per cent of total cases, if there has been no change in aggressiveness in obtaining histologic proof, this means that they saw approximately 1000 patients during this period In the 604 proven cases the operability rate was 55 per cent and the resectability rate 35 per cent During the period 1948 1955 there were 93 lobectomies and 127 pneumonectomies — a ratio of three to four The hospital mortality during this latter period was 6 4 per cent for lobectomies and 10 per cent for pneumonectomies The five year cumulative survival during this latter period was 33 per cent for lobectomies and 24 per cent for pneumonectomies These excellent results from surgical therapy seem to be due to careful selection of patients suitable for resection This conclusion seems justified when one considers that approximately 22 per cent of the total patients including both clinically and histologically proven cases were found suitable for resection The total salvage in terms of five year survival of all patients thus appears to be between 6 and 7 per cent

Boyd *et al* [6] in 1954, reported the experience of the Lahey Clinic with 403 patients with carcinoma of the lung seen during the previous 15 years Excluding diagnosis by cytology alone 301 of their cases or 75 per cent were histologically proven With the addition of 27 cases diagnosed by cytology, 328 (80 per cent) had positive diagnoses Fifteen patients lived five years or more This is 9 4 per cent of the total cases They reported one patient who had survived five years following x ray therapy alone Thirty-eight per cent of the patients who had been given what was thought to be a curative resection survived five years or longer Of 104 resect[illegible] 32 or 30 7 per cent

lobectomies The *total resection mortality* was a very creditable 7 6 per cent The operability (53 8 per cent) was high as compared to the resectability (25 8 per cent) indicating an aggressive surgical policy The price of this aggressive policy is shown by an 8 6 per cent mortality following exploratory thoracotomy It can be seen from this and subsequent reports that statistics from clinics and surgeons engaged in private practice may reflect a high salvage rate *in the treatment of bronchogenic* carcinoma This is probably due to some selection of patients more favorable for surgical therapy who are sent to these groups and individuals by referring physicians

Taylor and Waterhouse,[6] 1950, reported the combined experience of several surgeons in Great Britain in the surgical treatment of bronchogenic carcinoma Of 1,147 patients subjected to pneumonectomy, 52 7 per cent survived one year — 13 7 per cent five years Assuming a resectability rate of 35 per cent, this would indicate a 5 per cent salvage of all patients diagnosed

Ochsner[7] in 1954 reported his experience with 1,365 patients having bronchogenic carcinoma Forty-five per cent (619) were considered inoperable when first seen Of the remaining 746 patients 680 or 50 per cent of the total group underwent surgery (66 refused surgery), 442 or 32 4 per cent of the total group had pulmonary resections, and 84 or 19 per cent of these patients died following resection It is interesting to note that of the 238 patients who had exploratory thoracotomy without resection 42 died in the hospital, a mortality of 18 per cent In summary, 50 per cent of the patients had no surgery, 50 per cent had surgery, 33 per cent were resected and 17 per cent had thoracotomy without resection These figures are practically identical to those being reported by the authors Ochsner considered *74 per cent of his resections* to be palliative Of the untreated patients, less than 6 per cent survived one year Two patients, however, survived more than four years The price of total pneumonectomy was reflected in the high operative mortality (19 per cent) with three out of four deaths being due to cardiorespiratory complications Only 31 per cent of the patients survived one year following pneumonectomy and 15 per cent survived five years—a 6 6 per cent salvage of the entire group

Brock[8] in 1955 reported his experience *since 1947 with* radical pneumonectomy as a routine surgical procedure in the surgical treatment of bronchogenic carcinoma The operative procedure advocated by Brock results in a true en-bloc resection of the total lung, mediastinal pleura, lymph nodes, phrenic nerve with its accompanying vessels, and a pericardial cuff The pulmonary arteries and veins are secured intrapericardially as suggested by Allison[9] in 1946 This procedure was carried out in 145 patients Sixteen patients (11 per cent) died as a result of the operation Seventy two of the 129 patients who survived operation were still alive at the time of the report Of these 35 had survived over two years and the remaining 37 had survived varying *lengths of time up to two years* It was interesting to note that of the 29 patients surviving more than three years only 2 were found to have lymph nodes involved with neoplasm upon examination of the resected specimens Brock compared this series with 49 simple pneumonectomies *done by the* same group of surgeons during the same period of time In this group there was an 18 per cent operative mortality and only 18 per cent of the patients were still alive Since the basis of selection of patients on whom these pneumonectomies were *done is* not stated it is difficult to state whether the comparison of results is valid However the natural surgical inclination to apply the procedure of simple pneumonectomy to the poorer risk patients reserving radical pneumonectomy for the better risk patients with

more favorable lesions (only 2 of 29 patients surviving more than three years had involved lymph nodes) might explain the difference in results

Watson[9] in 1956 reported the experience at Memorial Hospital with the surgical treatment of bronchogenic carcinoma during the period from 1926 1955 A total of 2967 patients was seen during that time 2631 of them being seen since 1938 when the first total pneumonectomy was done at that institution The patients treated from 1949 55 were analyzed Exploratory thoracotomy for nonresectable lesions was found to have a mortality of 7 4 per cent (35 deaths in 470 cases) The resections were divided into radical pneumonectomy (125 cases with 13 6 per cent mortality) simple pneumonectomy (52 cases with 17 3 per cent mortality) and lobectomy and segmental lobectomy (50 cases with 8 per cent mortality) The five year survival rate of those cases eligible (1949 51) was 27 per cent for radical pneumonectomy 22 per cent for simple pneumonectomy and 25 per cent for selective resection Since Watson states the radical pneumonectomies were done for patients judged to be good risks and simple pneumonectomy was done for bad risk patients requiring chest wall pericardial and diaphragmatic resections the groups are not comparable In view of this selection of patients and a 5 per cent better mortality rate for lobectomy the survival rates do not support a contention that radical pneumonectomy accomplished substantially more than routine resection preserving pulmonary tissue whenever feasible

Collier *et al* reported the experience at the hospital of the University of Pennsylvania with 600 patients having carcinoma of the lung seen during a sixteen year period ending December 31 1955 Forty two per cent (256) were deemed to be inoperable Fifty eight per cent (344) had exploration of the chest and of these 226 or 38 per cent had resections Seventy four per cent of the resections were total pneumonectomies of the conservative type as compared to a radical pneumonectomy of the type described by Brock Lobectomy was done in 26 per cent The surgical mortality was 7 per cent Twenty five patients or 25 per cent of those resected survived a five year period The overall salvage rate for the entire group was 8 7 per cent Collier emphasized the importance of finding blood vessel invasion by the neoplasm as seen microscopically in the surgical specimen Only 6 per cent of the patients found to have blood vessel invasion survived five years as compared to 75 per cent who survived a similar period who did not have this finding Neuhof[7] had previously pointed out the importance of distant metastases due to blood vessel invasion in support of his contention that selective resection may be the operation of choice where possible in the treatment of bronchogenic carcinoma

Gibbon *et al*[4] in a recent paper reported the results of treatment of 353 patients with histologically proven primary carcinoma of the lung treated during the period 1946 51 Thirty per cent (107) were considered inoperable 29 per cent or 101 patients underwent thoracotomy without resection and 41 per cent or 145 patients had resections Seventy per cent operability and 41 per cent resectability rates are higher than reported by most workers and are undoubtedly due to consideration of only histologically proven cases A total pneumonectomy was done in all but 9 cases This radical surgical policy is reflected in the 23 per cent surgical mortality Thirty patients having resections survived five years (21 per cent of the resected group) The lobectomies were not done by design but because of a mistaken impression that the lesion being removed was benign Two of 9 patients thus treated survived five years felt that extension of the lesion

lung was the single most important factor influencing survival Cell type seemed less important No patients having resection of a portion of involved chest wall survived more than 18 months Four patients considered to be inoperable had survived five years 2 after exploration followed by x-ray therapy *The over all five year survival of* 34 out of 353 patients (9 6 per cent) is considerably higher than reported by most workers and reflects the selection of material in favor of the surgical cases

Burford[14] has reported the survival rates following treatment of 1008 patients all with histologically proven bronchogenic carcinoma that were seen by him and his associates at the Barnes Hospital between January 1, 1948 and December 31, 1955 Forty per cent (405) of the patients were considered inoperable or refused surgery Sixty per cent or 356 of the 603 patients considered operable had resections — a resectability rate of 35 per cent Pneumonectomy was the preferred operation although 20 per cent of patients had lobectomies because of considerations of pulmonary function and cell type (bronchiolar carcinoma) The mortality following exploratory thoracotomy without resection was 9 per cent The pneumonectomy mortality was 13 per cent and that of lobectomy 12 per cent Of the 461 patients followed who were eligible 40 (22 per cent) survived five years There were no 5 year survivals in inoperable or nonresectable patients The overall salvage rate was 9 per cent It is interesting to note the similarity of these percentage figures to those of Gibbon[12] who also reported only histologically proven cases

The summaries of reports made by various workers of results of treatment of bronchogenic carcinoma given above is not intended as a comprehensive review of the literature on this subject These reviews have been included by the authors to provide a background for the reporting of the own results

AUTHORS' SERIES

We have analyzed the results of treatme of 1180 patients seen by us who were dia nosed as having bronchogenic carcinon during the period from 1945 1957 In 7 per cent of these patients we obtained histo logic proof of the diagnosis while in the r maining 30 per cent clinical evidence su ported by observation of the patient s cour seemed sufficient to warant a diagnosis c malignant bronchial neoplasm One ha (50 5 per cent) of the patients were foun to be not suitable for surgical therapy Th other half (49 5 per cent) had surgery *Thirty-five per cent of the total group ha* resections and 15 per cent underwent ex ploratory thoracotomy without resectio (Table I) The operative mortality for re sections was 6 per cent with the mortality for pneumonectomy 9 per cent and that of lobectomy 3 per cent The 420 resections *were almost equally divided* between pneumonectomies (214) and lobectomies (206) Exploratory thoracotomy for non resectable lesions in our hands carried a mortality of 2 8 per cent (5 deaths in 177 patients) Thirty eight patients of those eligible survived a five year period a salvage rate of 6 5 per cent If only histologically proven cases are considered as a base line for determining the salvage rate the figure would be 9 2 per cent Although there is

TABLE I

OPERATIVE MORTALITY FOR BRONCHOGENIC CARCINOMA 1945 1957

Type of Operation	*Number*	*Deaths* Number	*Deaths* Per cent
Resections			
Pneumonectomy	214	19	9 0
Lobectomy	206	7	3 0
Total	420	26	6 0
Exploratory Thoracotomy	177	5	2.8

Total patients seen 1180 resectability rate 35 per cent, exploration rate 15 per cent.

indication that by better application of presently available modalities of treatment this overall salvage rate may be improved, because of the biologic nature of bronchogenic carcinoma, the percentage improvement will be small

FIVE YEAR SURVIVORS

Seventeen patients survived five years following pneumonectomy, 18 following lobectomy, and 3 following exploration and subsequent irradiation therapy Of these 5 survived more than ten years and 16 more than eight years without evidence of recurrence of disease One patient who survived more than ten years following right pneumonectomy developed a new primary bronchogenic carcinoma in the left lung to which he succumbed One patient who survived five years following pneumonectomy died of metastatic carcinoma from the original neoplasm Three additional patients among the five year survival group have died of unrelated causes five, seven, and seven years respectively following resection One of these patients was 75 and another 83 years of age at the time of death

Ten of the patients surviving five years following pneumonectomy and two following lobectomy (one with bronchoplastic reconstruction of the airway) had hilar lesions that were bronchoscopically visible prior to resection The prevalent opinion that patients having hilar carcinomas are incurable is therefore not justified Metastatic carcinoma was found in the hilar and mediastinal nodes in seven patients that had pneumonectomies and in two that had lobectomies There was invasion by neoplasm of the peribronchial nodes in many of the other surviving patients Admittedly lymph node invasion is a finding indicating a poorer prognosis for long survival but with adequate resection of the involved regional nodes cure is still possible

Only 8 of the 38 patients who have survived five years following resection were asymptomatic prior to surgery Fifteen had had symptoms less than six months and 15 more than six months In the latter group 6 had had symptoms more than a year and 4 more than two years

The survival of patients whose length of symptoms indicated the presence of the neoplasm for many months prior to resection indicates that the time factor is only of relative importance in the surgical treatment of bronchogenic carcinoma and that the biologic nature of the neoplasm plays a greater role in determining the chance of survival

Twenty-nine of the 38 patients surviving five years had epidermoid carcinoma Of the remaining, 6 patients had adenocarcinomas and 1 a bronchiolar carcinoma Two patients having small cell undifferentiated carcinomas survived five years following irradiation therapy given after exploratory thoracotomy These results merely reflect that in general the chance of survival is best with the differentiated neoplasms and that since the greater number of bronchogenic carcinomas are differentiated squamous ce carcinomas the majority of long term sur vivors will have had this type of lesion It is significant, however, that there were no five year survivors following resection in patients having undifferentiated neoplasms

QUALITY OF SURVIVAL

Quality of survival is equally as important as length of survival but is less subject to statistical analysis However, of the 17 patients who survive five years following total pneumonectomy 6 are dyspneic to the degree that they are almost completely disabled by their poor pulmonary function The remaining 12 patients lead reasonably active lives One of the 18 patients who survived five years following lobectomy — a 75 year old man — succumbed to respi ratory inadequacy but he was dyspneic the time of surgery and would not tolerated [illegible] nectomy T

ditional patients in the lobectomy group who were somewhat dyspneic before surgery are now forced to live restricted lives because of poor pulmonary function The remaining 15 patients have no important physical restrictions and lead active productive lives Such comparisons with small groups of patients are somewhat meaningless There is no doubt, however, that total pneumonectomy is a crippling operation and that the quality of survival following lobectomy from the standpoint of pulmonary function is superior to that following pneumonectomy

SURVIVAL RATES IN INOPERABLE PATIENTS

We were able to obtain accurate follow-up information on 319 of the 400 patients who during the period from 1945 55 were either considered inoperable or did not return for treatment Of these 87 per cent (279) survived less than one year (Fig 1) Of the 13 per cent who survived one year only 6 or 2 per cent were alive at the end of two years Two patients have survived four years although one has since died It may be significant that both of these patients received irradiation therapy

SURVIVAL FOLLOWING EXPLORATORY THORACOTOMY

One hundred forty three patients during the period from 1945-57 had exploratory thoracotomies and were found to have nonresectable lesions The fate of 124 of these patients is known One hundred three or 84 per cent did not survive one year Of the 21 who survived one year only 5 (4 per cent) were alive at the end of two years Three (3 per cent) survived five years or more and 2 are still living — one twelve years and the other eight following exploration in which tissue removed gave pathologic proof of a malignant bronchial neoplasm All three patients who survived five years received irradiation therapy by conventional techniques (See Chapter on radiation Therapy)

It is interesting that the survival curv (Fig 1) of patients deemed to be i operable and those found to be nonresec able at the time of operation are practical identical This is true even when the fi year of survival is broken down into qua ters (Fig 2)

Taylor[6] reports that 31 per cent of pa tients having exploratory thoracotomies d within three months following surgery an concludes that this poor survival time is du to injury caused by surgery If one grant that as a group patients chosen for surgic therapy and found to be nonresectabl should have a longer survival because dis semination is not obvious as it is in man patients considered to be inoperable ou data would tend to support this conclusion The conclusion is justified, at least, tha thoracotomy for the nonresectable lesion carries a definite mortality (3 per cent in the authors' series) with no benefit and possible shortening of survival when com pared to inoperable lesions The only ad vantage that can be claimed is pathologic proof in the diagnosis of the indeterminate lesion Other methods of obtaining this proof, such as bronchoscopic examination cervico mediastinal exploration and needle biopsy may be preferable The authors strive to maintain a rate of 10 per cent or less of all patients for exploratory thoracotomy without resection

SURVIVAL FOLLOWING RESECTION

Four hundred twenty of the 1180 patients seen during the period from 1945 57 have had surgical resection of their neoplasms. Two hundred fourteen patients had pneumonectomies and 206 lobectomies Three hundred seventy five of these resections were done more than a year ago Of these 193 were pneumonectomies and 179 lobectomies The fate of all of these patients

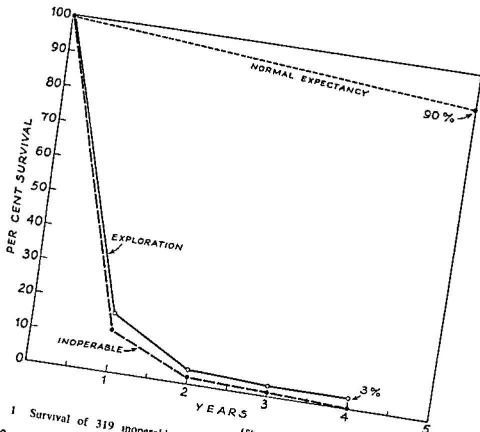


Fig 1 Survival of 319 inoperable patients and 124 patients having exploratory thoracotomy for bronchogenic carcinoma (Shaw Paulson and Kee 1945 57)

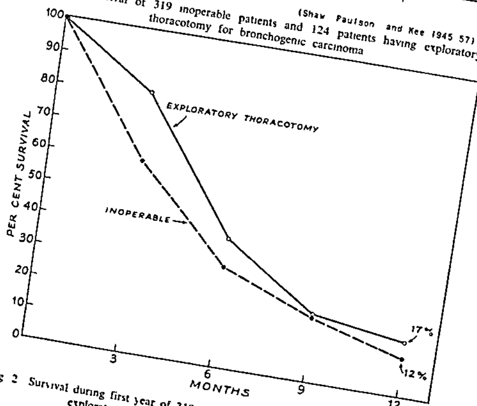


Fig 2 Survival during first year of 319 inoperable patients and 124 patients h exploratory thoracotomy for brc carcinoma (Shaw, Paulson, and Kee)

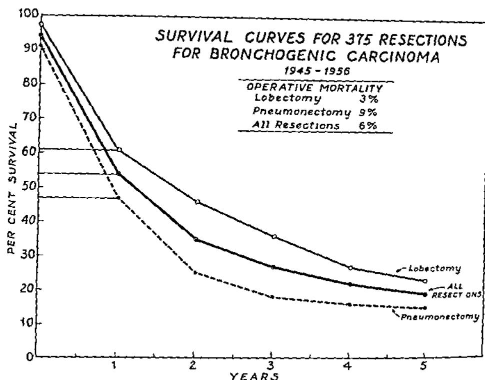


Fig 3

is known Fifty four per cent of all patients having resection survived one year 35 per cent survived two years and 19 per cent five years Sixty one per cent of the patients having lobectomies survived one year as contrasted to only 46 per cent of the patients having total pneumonectomy The corresponding figures for two years were 46 per cent and 27 per cent At the end of five years 23 per cent of the lobectomy patients and 15 per cent of the pneumonectomy patients were still alive Combining the two groups 19 per cent of patients having resection survived five years without sign of recurrence of neoplasm The survival curves (Fig 3) indicate that the prognosis following lobectomy is somewhat better than that following pneumonectomy This is undoubtedly due to the inclusion in the lobectomy group of many of the more favorable lesions No one would seriously challenge the fact that as a group the quality of survival of the patients having only lobectomies is superior to that of the patients who have lost an entire lung The fact that in both groups approximately one half of the patients did not survive one year indicates that this poor survival was due to factors not related to the type of resection but rather to the biologic nature of the disease

The survival curves for patients having resections for bronchogenic carcinoma follow the same pattern as curves of survival following surgery for neoplasm elsewhere in the body The percentage chance of survival after two years becomes increasingly good and approximates the survival curve of the general population of the same age group The pneumonectomy patient who survives three years appears to be in a more favorable position from the standpoint of survival than the patient treated by lobectomy This is probably due to the selective factor of the increased mortality operating in the first three year period since at the end of five years only 15 per cent of the

pneumonectomy group were alive as compared to 23 per cent of the lobectomy patients

FACTORS AFFECTING SURVIVAL FOLLOWING RESECTION

Influence of Pathologic Type on Type of Surgery and Survival

If one disregards general factors such as age, sex and certain morbid conditions, the pathologic type of tumor is the single most important factor influencing survival time. This factor is first reflected in the influence it has on the type of surgery (Table II). Sixty per cent of the patients having a neo- plasm of the differentiated squamous cell ype were resectable. Thirty-three per cent f patients with this cell type had pneu- onectomies and 27 per cent lobectomies. le preponderance of pneumonectomies is e to the tendency of this type of lesion quently to have its origin in major bronchi and to infiltrate locally. The resectability

TABLE II

Resectability Rates for 736 Proven Cases of Bronchogenic Carcinoma. Total Cases 1055. 1945-1956

Cell Type	*Resectability Percentage*	*Type of Resection Pneumonectomy*	*Lobectomy*
Squamous cell	60%	33%	27%
Adenocarcinoma	45	14	31
Small cell undifferentiated	24	15	9
Large cell undifferentiated	52	24	28
Bronchiolar	45	0	45
Total	51	26	25

rate was 45 per cent for adenocarcinomas. With this cell type lobectomies were more frequent, 31 per cent as compared to 14 per cent for pneumonectomy. This reflects the tendency of adenocarcinomas to develop in the peripheral portions of the lung. Bronchiolar carcinomas could be resected by lobectomies or even segmental resections in 45 per cent or not at all. This type of pulmonary neoplasm may remain as a localized tumor in the periphery of the lung for a long period of time. Contrariwise in an almost asymptomatic patient it may be detected as a widespread bilateral infiltration wholly unsuitable for surgical therapy. Small cell undifferentiated carcinomas were resectable in only 24 per cent of cases. Fifteen per cent had pneumonectomies and 9 per cent lobectomies. In the majority of instances in this type of lesion the resection was carried out before the pathologic type could be determined. The small cell undifferentiated carcinoma is usually unsuitable for surgery because of rapid dissemination.

The survival rates for five years of those patients treated by resection were 17 per cent for the squamous cell carcinoma, 22 per cent for the adenocarcinoma, and none for the small cell undifferentiated carcinoma (Fig. 4). Of the entire group, including the inoperable and nonresectable lesions, 9.4 per cent of those patients having a squamous cell carcinoma, 10.0 per cent of the group with adenocarcinoma, and 3.3 per cent of those with a small cell undifferentiated carcinoma survived five years. There were three patients whose lesions were operable but not resectable, proven pathologically, who lived seven to twelve years after irradiation therapy. Two of these patients had small cell undifferentiated carcinomas and one had a squamous cell carcinoma. (See Chapter on Irradiation Therapy.)

Chest Wall Invasion

We do not share the generally expressed pessimism in regard to survival following resection of peripheral neoplasms that have invaded the chest wall (Fig. 5a and b). Forty five patients having pulmonary resections also had resection of a portion of the involved chest wall in an en-bloc resection. Bronchial neoplasms that invade the chest wall more often can be adequatel excised with a selective pulmonary resec Of 45 patients only 11 re

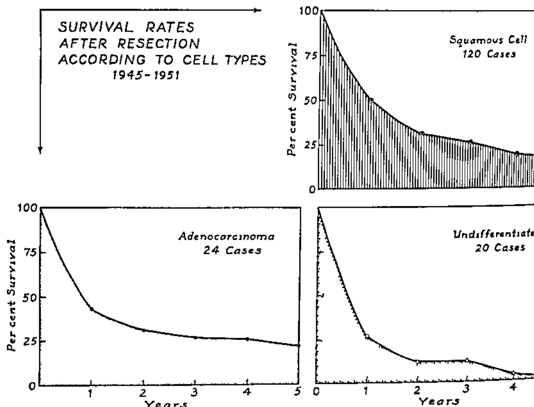


Fig 4

total pneumonectomy In 12 patients a segmental resection was done The remaining 22 patients had lobectomies There was no surgical mortality in this group

Twenty one of 38 eligible survived eighteen months or more Gibbon[15] reported that they had no patients surviving more than eighteen months in whom it was necessary to resect a portion of the involved chest wall It may be significant that only 2 of the 11 patients surviving had total pneumonectomies the remainder having lobectomies or segmental resections Seven patients or 20 per cent have survived three years and of these 6 are still living, one over six years following a right lower lobectomy One patient died four and one half years following resection of the apicoposterior segment of the left upper lobe along with a portion of the dome of the involved chest wall Death was due to carcinoma in the right lung that on post mortem examination was thought to represent a new mary neoplasm The survival curve (6) of these patients seems to depart little from that of all patients treated surgical resection of a bronchogenic c noma

BRONCHOPLASTIC PROCEDURE

The use of bronchoplastic procedure the surgical treatment of bronchogenic cinoma in the interest of preservation lung tissue is an innovation and for reason the results following this type of section will be recorded in more detail use of this technique may be mandat when applying surgical resection in a pati who could not tolerate total pneumon tomy because of poor respiratory functi The deliberate use of this technique as adequate cancer operation is justified in attempt to improve the quality of survival patients with adequate pulmonary functi

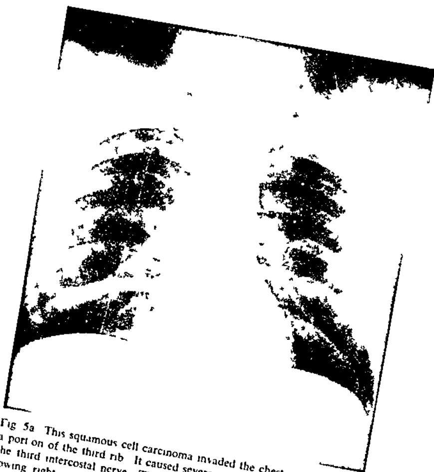


Fig 5a This squamous cell carcinoma invaded the chest wall destroying a port on of the third rib It caused severe pain along the distribut on of the third intercostal nerve The patient is alive and well five years fol lowing right upper lobectomy includ ng en bloc resection of a port on of the chest wall



Fig 5b Right upper lobe with resected portion of chest wall showing invasion of the third rib and intercostal nerve by the neoplasm

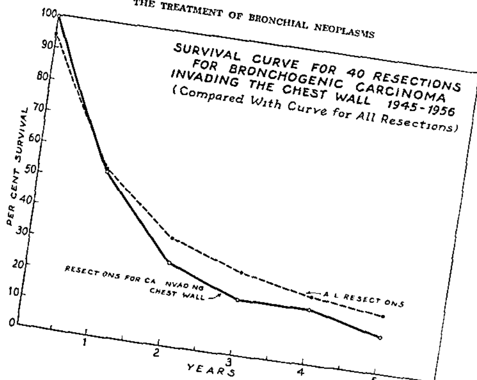


Fig 6

) patients had bronchoplastic pro cedures in an extension of the usual limits of resectability for reasons of palliation In both the left bronchus was anastomosed to the trachea following resection of the right lung along with the carina One died on the twelfth postoperative day due to insufficient pulmonary function but the other survived year in reasonable comfort

Sixteen patients have had bronchoplastic procedures to avoid removing the total lung here was no mortality Two patients de oped empyemas postoperatively which led with rib resection drainage In the patients twenty three lobes were pre served

The procedure was indicated in seven patients because of poor pulmonary func tion Two patients died at four and six months due to recurrence of carcinoma at the site of anastomosis and one succumbed to spinal metastases nineteen months follow ing surgery Lymph node metastases were found in all three at the time of resection The four remaining patients are alive and relatively comfortable considering their re duced respiratory function fifteen months three years three and one half years and five years following surgery Lymph node metastases were found at the time of surgery in only one of these patients — the one who has survived five years

In the other nine patients bronchoplasty was performed deliberately as an adequate cancer operation There was recurrence of neoplasm at the site of the anastomosis in one of these patients whose right lower and middle lobes were preserved following upper lobectomy This patient died three years following surgery Three additional patients in this group have died two and one half three and four years respectively following surgery None of these deaths could be ascribed to the type of technique employed The remaining five patients are alive a normally active without evidence of r

rence eight months, two and one-half years, three years and three and one-half years following surgery

It is difficult to draw sound conclusions from the fate of 16 patients All had hilar lesions Included in the group are several patients having small epidermoid carcinomas that had blocked major segmental bronchi which gave rise to symptoms leading to their detection while in a localized state Six patients, however, had positive evidence of invasion of hilar lymph nodes resected at the time of surgery The inclusion of the patients with poor pulmonary function (one of whom had previously had a seven rib thoracoplasty on the opposite side for treatment of pulmonary tuberculosis) probably makes this group fairly representative of hilar lesions in general In consideration of these facts it is gratifying that 14 of the 16 patients (88 per cent) survived one year, and 11 of 14 (80 per cent) patients eligible survived two years The corresponding percentages of survival of all our patients having resections were 54 per cent for one year and 35 per cent for two years All patients with the exception of those dyspneic prior to surgery have adequate respiratory capacity for active living (Fig 7)

Recurrence at the site of anastomosis was more frequent (3 out of 7) in patients in whom the right lower and middle lobes were preserved by anastomosing the intermediate bronchus to the right bronchial stump close to the trachea The bronchial section in these cases was as high as could be obtained in doing a right total pneumonectomy Adequate resection of a carcinoma which is involving the bronchial wall in the region of the right upper lobe orifice is difficult by any technique because of the short right main bronchus Recurrence at the anastomotic site occurred in 1 patient who had anastomosis of the left upper lobe bronchus to the left main bronchus performed as a compromise with poor pulmonary function but did not occur in 3 other patients in whom the same procedure was used in removing smaller neoplasms

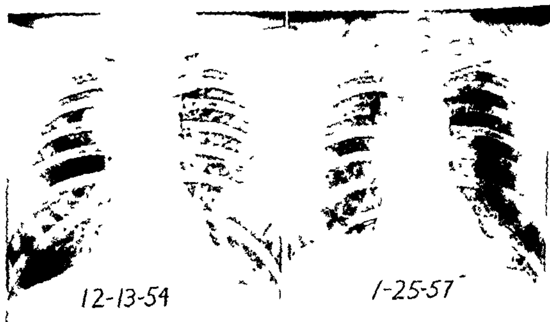


Fig 7 An adequate resection of this large squamous cell carcinoma was accomplished by utilizing a bronchoplastic procedure to preserve the lower and middle lobes The patient is working daily without disability three years following surgery

This experience with bronchoplastic procedures to preserve pulmonary tissue in selected patients is encouraging and seems to deserve a continuing trial

PULMONARY NODULES

The most favorable morphologic type of bronchogenic carcinoma for resectional therapy is the one that presents as a pulmonary nodule Unfortunately only 10 per cent of all patients seen fall in this group These lesions not only can usually be removed by a selective resection but also represent the most favorable lesion from the standpoint of survival

One hundred two patients had bronchogenic carcinomas that presented as pulmonary nodules Twenty of these patients were inoperable either because of the presence of distant metastases or because of poor pulmonary function Eighty two patients were operable and in only one of these was resection not advisable because of gross mediastinal involvement Of the 81 patients who had resections 10 had total pneumonectomies, 62 lobectomies, and 9 segmental lobectomies There was 1 death, a surgical mortality of 1 2 per cent This was due to cardiac arrest occurring following completion of a right upper lobectomy The

TABLE III

SURGICAL STATUS OF 102 PULMONARY NODULES DUE TO BRONCHOGENIC CARCINOMA

Status		No Cases
Inoperable		20
Distant metastases	15	
Poor pulmonary function	4	
Refused surgery	1	
Operable—With evidence of node involvement		21
Lobectomy	14	
Pneumonectomy	6	
Exploration	1	
Operable—Without evidence of node involvement		61
Segmental lobectomy	9	
Lobectomy	48	
Pneumonectomy	4	
Total		102

One death following lobectomy due to cardiac arrest (1 2%) Shaw Paulson and Kee 1945 57

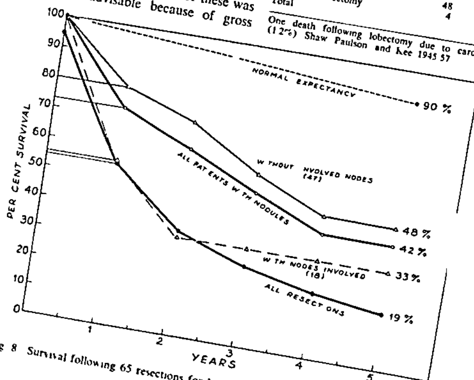


Fig 8 Survival following 65 resections for bronchogenic carcinoma in patients having pulmonary nodules

were no major surgical complications (Table III)

Sixty five patients had resections more than a year ago and the fate of these patients is known Survival percentages using the life table method were for one year, 73 per cent, two years 63 per cent, three years, 52 per cent, and for four and five years, 42 per cent (Fig 8)

Eighteen patients were found to have lymph node metastases at the time of resection This finding seriously prejudiced the chances of survival since only 55 per cent survived one year and 33 per cent two years Those eligible to survive beyond two years, however, are still alive — 3 for three years 2 for four years, and 1 for five years following resection (Fig 8)

The survival rate of the 47 patients in whom no nodal metastases were found was much better Eighty one per cent survived one year Again using the life table method the rates were for two years, 73 per cent, three years 58 per cent four and five years, 48 per cent (Fig 8)

The presence or absence of symptoms that could be attributed to the nodule was of prognostic significance Forty five patients had nodules resected which caused symptoms Sixty six per cent of those resected less than two years ago were still alive but only 30 per cent of those resected more than two years ago still survived (Table IV) In contrast 80 per cent of the patients having asymptomatic nodules resected less than two years ago are still living and 70 per cent of those resected more than two years survive (Table V)

In summary a patient who has an asymptomatic nodule due to bronchogenic carcinoma who at the time of surgery is found to have no lymph node involvement can have the neoplasm resected by lobectomy with minimal risk and with a two out of three chance of surviving five years without evidence of recurrence (Fig 9a and b)

SUMMARY

Evaluation of results of treatment of bronchogenic carcinoma considering all types found in a series as a single unit leads to misleading conclusions and may foster an attitude of therapeutic nihilism that is not justified One cannot compare the results of treatment in unlike cases using solely the criterion of time of survival The life history of a small cell undifferentiated carcinoma cannot be compared to that of a bronchiolar or well differentiated epidermoid carcinoma because both are neoplasms any more than the life span of a field mouse can be compared to that of an elephant though both are mammals The bronchial adenoma meets all of Virchow's tenets for neoplasm but was removed from the general classification of bronchogenic carcinoma because of this factor of difference in life history

TABLE IV

SURVIVAL FOLLOWING RESECTION OF 45 SYMPTOMATIC PULMONARY NODULES DUE TO BRONCHOGENIC CARCINOMA

Period Since Resection	*Number of Resections*	*Number Alive*	*Per cent Surviving*
Less than 1 year	9	5	66
1 year	9	7	
2 years	8	2	30
3 years	11	3	
years	1	0	
years or more	7	3	
Total	45	20	

Two deaths were due to causes other than bronchogenic carcinoma Shaw Paulson and Kee 1945 57

TABLE V

SURVIVAL FOLLOWING RESECTION OF 36 ASYMPTOMATIC PULMONARY NODULES DUE TO BRONCHOGENIC CARCINOMA

Period Since Resection	*Number of Resections*	*Number Alive*	*Per cent Surviving*
Less than 1 year	7	6	80
1 year	8	6	
2 years	4	4	70
3 years	6	2	
4 years	3	3	
5 years or more	8	6	
Total	36	27	

Three deaths were due to causes other than carcinoma. Shaw Paulson, and Kee 1945 57

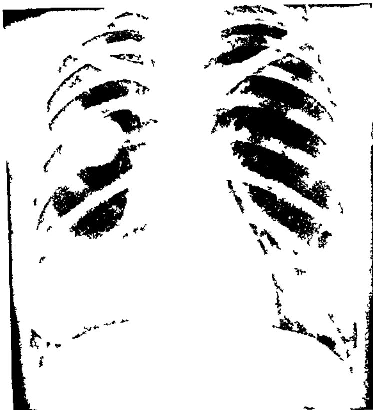


Fig 9a This large asymptomatic pulmonary nodule was discovered by a routine x ray of the chest in the right upper lobe of a 52 year old woman The patient is alive and well two years following lobectomy She now has practically a normal life expectancy for her age and sex



Fig 9b Resected right upper lobe containing a typical squam cell carcinoma presenting as a large pulmonary nodule

Surgery can be usefully employed for the removal of biologically early neoplasms The surgery should be carried out with maximum preservation of pulmonary function Radical pneumonectomies may of necessity be required to encompass large locally infiltrating neoplasms but in the usual case simple pneumonectomy or lobectomy with dissection of mediastinal and hilar lymph nodes are adequate cancer operations The survival of patients suitable for surgical therapy should not be compared with that of inoperable patients inferring that surgical therapy was responsible for the increased time of survival They are totally unlike series of cases The only justification for comparing survival in such unlike series is to place in proper perspective the prognosis of a patient in respect to the group within which he falls Bronchogenic carcinomas that have extended to the general lymphatics are no more a surgical entity than Hodgkin s disease and once they have invaded the blood stream as evidenced by distant metastases are no more curable by surgical therapy than leukemia The surgeon should be vigilant in his search for lesions suitable for surgical therapy but judicious in the decision to apply surgery so as to avoid harming patients who cannot be benefited by this modality of treatment

The uniformity of the results reported by various authors emphasizes the major role played by the biologic nature of bronchogenic carcinoma in the overall prognosis of treatment of this disease Approximately one half of patients are inoperable when first diagnosed and only one third have lesions that can be resected Studies of series of patients incorporating a broad base with inclusion of clinically diagnosed cases with those histologically proven indicate that a salvage of approximately six per cent of all patients as evidenced by five year survival is being accomplished by present methods of treatment If only histologically proven cases are considered the salvage rate is approximately 9 per cent Increasing the scope of surgery by radical resections has not improved this survival rate This is due not only to the biologic nature of the disease but the fact that factors resulting due to radical resections tend to lessen the period of survival On the other hand a patient having an asymptomatic neoplasm presenting as a peripheral pulmonary nodule with no evidence of nodal metastases has a 70 per cent chance of five year survival following resection Unfortunately less than 10 per cent of a total series of bronchial neoplasms will fall within this favorable classification The finding of more patients with biologically early neoplasms should increase the survival rate but this increase will be limited by the very nature of the disease

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Bronchial Adenoma

By John Lester Kee, Jr M D

INTRODUCTION AND HISTORY

THE ADENOMA OF THE BRONCHUS is one of the most interesting of the primary bronchial neoplasms and for many years has been the subject of a great deal of discussion and controversy The first report of one of these tumors was made by Mueller in 1882[1] This was a case of a benign pedunculated adenoma with partial calcification found post mortem in the left main bronchus of a woman aged 22 who had suffered eight years from profuse expectoration of blood and foul sputum At autopsy there were marked bronchiectatic changes in the bronchus distal to the site of the adenoma Following this report there were occasional reports of adenomas found either at autopsy or by bronchoscopic examination but it was not until 1932 that these tumors were established as a recognizable clinical entity by Wessler and Rabin[2] Since that time many cases have been reported and much has been learned about the natural history and behavior of this tumor

There have been three main areas of disagreement in regard to the adenoma These disputes have centered around the proper terminology, the cellular origin and the degree of malignancy In this discussion we have used the term "adenoma" to apply to the whole group of tumors The term "bronchial adenoma" is used to include the carcinoid and cylindromatous types which will be considered individually in the discussion of the clinical or pathological aspects in which they differ This terminology is not used because it is necessarily best but because it is the most generally accepted The term "adenoma" was first used by Mueller[1] and has been the one most widely used by most authors for the entire group of tumors although some have used this term for the carcinoid type alone There is a real objection to calling these tumors "adenomas" since this term implies a benignity which is not always characteristic of these neoplasms Other names which have been used are *polypoid adenoma, basal cell carcinoma* adenomatous polyp benign glandular bronchogenic tumor, vascular adenoma, mixed tumor, grade I adenocarcinoma, and malignant adenoma The term cylindroma' was first applied by Billroth in 1859 to a tumor of the paranasal sinus invading the orbit[3] The similarity between these tumors arising in the accessory nasal sinuses and those in the bronchial tree was recognized and the same term used for these tumors It was thought that they occurred wherever major or minor salivary glands or simple mucous glands were found[4] In recent years as more data have been collected concerning the carcinoid and cylindromatous adenomas it has been increasingly apparent that there is a definite difference between these tumors in rega[rd] to their location, degree of malignanc[y] response to treatment In spite

differences, however, these two tumors are closely related and cause similar clinical manifestations Because of differences in natural history and prognosis, it is of importance that these tumors be recognized and a sharp distinction made between them and bronchogenic carcinoma

THEORIES OF ORIGIN

There have been many theories suggested to explain the origin of adenomas and the variations seen in the cellular pattern Heck[6] (1916) advocated origin from embryonic buds or non developed foci of lung anlages Wessler and Rabin[4] believed that the adenomas originated in the duct epithelium of mucous glands because (1) the tumors are covered by intact epithelium and lie on an uninterrupted basement membrane, and (2) their cellular elements do not resemble elements of mucous glands and no apparent transition from normal mucous glands could be seen Hamperl[6] and Stout[7] believed that the adenomas arose from the peculiar cells known as 'oncocytes' or 'pyknocytes' which are found in mucous and serous glands and their ducts Crafoord and Lindgren[8] placed the bronchial adenomas with the mucous and salivary gland tumors recognizing their characteristic slow growth as well as a tendency toward 'local malignancy,' i e, local invasion of surrounding structures Because of a certain resemblance of some of the adenomas to fetal lung tissue Womack and Graham[9] suggested that they were associated with failure of the embryonic buds to develop into normal structures and termed these tumors "mixed tumors" of the lung They believed that they were formed of both entodermal and mesodermal elements and regarded them as potentially malignant They considered them similar in behavior and origin to the mixed tumors of the parotid gland After years of controversy it is now generally acknowledged that bronchial adenomas have their origin in the mucous glands and their ducts in the bronchial walls

MALIGNANCY

For many years there was considerable disagreement over the malignancy of the adenomas Some writers believed them entirely benign, some considered them benign but capable of undergoing a malignant change, and still others considered them to be malignant tumors which grow very slowly and metastasize late in their course There is now ample evidence that these tumors do grow slowly, are locally invasive and also may metastasize to lymph nodes, mediastinum, vertebrae, and liver Numerous authors[10] have reported cases of metastatic adenomas and have shown that the adenomas of the cylindromatous type are much more likely to metastasize than the carcinoid adenomas McBurney, Kirklin, and Woolner[10] reported 87 instances of bronchial adenoma with metastases stating that ten per cent of all adenomas metastasized They believe that the histopathologic picture may indicate that a given adenoma may have metastasizing qualities None of the adenomas in the Mayo Clinic series that had perfectly regular carcinoid pattern and little or no pleomorphism or mitotic figures metastasized distantly In two cases such adenomas did metastasize to lymph nodes In those tumors that metastasized distantly the carcinoid pattern was not orderly Pleomorphism mitotic figures and irregular cell pattern were more frequent Adenomas of the cylindromatous type were three times as likely to metastasize as those of the carcinoid type In our series of 35 cases 4 showed evidence of local invasion and 3 had distant metastases Of the 3 patients who had distant metastases, i e, metastases to cervical nodes diaphragm, or contralateral lung, 2 patients had tumors which were histologically of the cylindromatous type

INCIDENCE

Adenomas are said by various authors to comprise between 6 and 10 per cent of all primary lung tumors Only 3 per cent of our 1215 primary bronchial tumors were adenomas Adenomas are found more frequently in women than in men in contrast to bronchogenic carcinoma In our series, adenomas were found almost twice as frequently in women as in men (23 females 12 men) The average age of our patients when seen for treatment was 42 years with the majority of the patients in the 30-39 year age group (Table I) The greatest number of these patients noticed the onset of symptoms between the ages of 20-30 years and had had symptoms for an average of six years at the time they were first seen These figures do not differ greatly from larger collected series of adenomas but are strikingly different from the figures for bronchogenic carcinoma There were 33 white patients, 1 American Indian and 1 Negro in this group The youngest patient was 14 years old while the oldest was 65

LOCATION

Adenomas are most frequently found arising from the bronchial wall of one of the

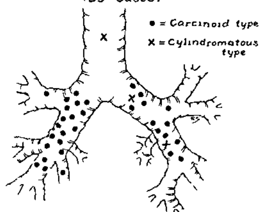


Fig 1 Location of adenomas in the tracheobronchial tree

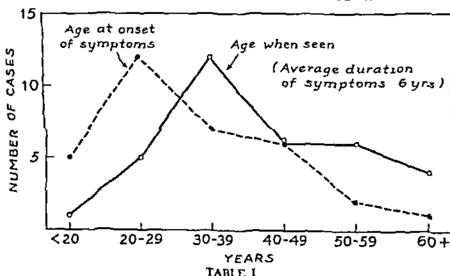


TABLE I

Age of patients at onset of symptoms and age when seen The average duration of symptoms was six years

major bronchi For this reason a very high per cent are visible by bronchoscopic examination and accessible for biopsy In our series 80 per cent were located in the major bronchi where they could be seen by means of bronchoscopy (Fig 1) Since the glandular elements from which the adenomas arise are found as far out into the bronchial tree as the cartilage extends, i e, to a diameter of 1 mm,[11] theoretically tumors arising in these glands may be found quite far out in the periphery of the lung Maier found 10 per cent to be located peripherally[12] However, these tumors are most frequently seen in the major bronchi probably because the glands are more numerous in the larger bronchi In our series only two tumors were seen on roentgenograms as pulmonary nodules, i e, a peripheral nodule surrounded by lung parenchyma The cylindromatous type is more likely to occur near the coryna or in the trachea while the carcinoid adenoma rarely if ever involve the trachea

GROSS PATHOLOGICAL AND BRONCHOSCOPIC APPEARANCE

Grossly the adenoma is usually found as a polypoid or sessile, lobulated mass protruding from or through the bronchial wall The intrabronchial portion frequently constitutes only a small part of the tumor mass with the major portion being in the peribronchial region At the time of operation the tumor may be felt as a soft to moderately firm peribronchial mass which can be separated without great difficulty from the surrounding lung and mediastinum but with a very firm bronchial attachment Through the bronchoscope the adenoma may be seen as a pinkish or reddish lobulated intrabronchial structure covered by intact bronchial mucosa Because of the great vascularity of these tumors, serious bleeding may result from biopsy and even exsanguination has

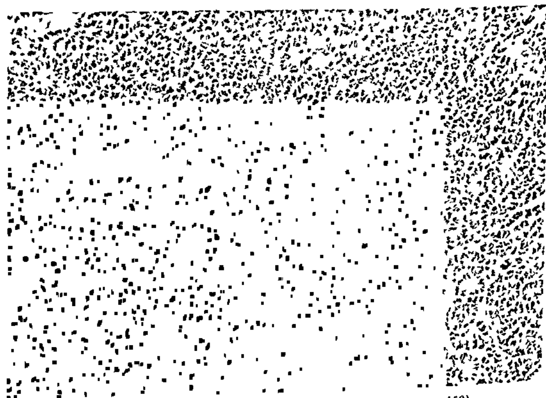


Fig 2 Photomicrograph of a typical carcinoid adenoma (×150)

been reported following biopsy[11] For this reason, many surgeons prefer not to biopsy any tumor that has the typical bronchoscopic appearance of an adenoma The cylindromatous adenomas seen in the trachea may show more evidence of ulceration and be more diffusely situated over the tracheal wall There may be marked bronchiectatic changes and destruction of lung tissue due to the presence of chronic infection distal to partial or complete obstruction of the bronchus

MICROSCOPIC APPEARANCE

The carcinoid pattern is found microscopically in 90 per cent of the adenomas These tumors are composed of small uniform cuboidal cells which contain a moderate amount of very finely granular eosinophilic cytoplasm and are arranged in strands sheets or in acinous formation (Figs 2 and 3) The nuclei are round or oval deeply staining and usually centrally placed There is little pleomorphism and mitoses are absent in the well-differentiated carcinoid pattern These tumors resemble the carcinoid tumors of the small intestine but argentaffin granules have rarely been demonstrated [illegible]

The cylindromatous type of adenoma is composed of small cells with darkly stained round or oval nuclei (Fig 4) There is a moderate amount of clear cytoplasm present The cells are arranged in branching masses forming tubules or in groups forming irregular spaces which are filled with mucoid secretion Mitoses are rarely seen except in actively infiltrating areas This tumor is much more likely than the carcinoid type to invade locally as well as to have distant metastases The only late deaths in our series were in two patients who had the cylindromatous pattern In a series of cases reported by Enterline and Schoenberg

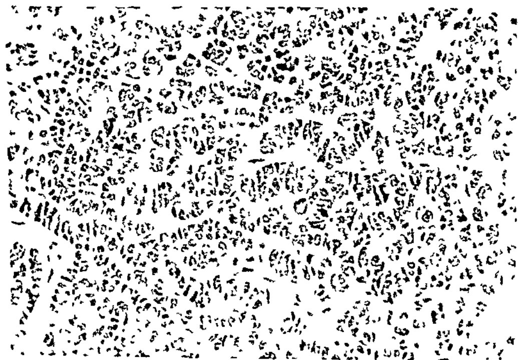


Fig 3 Higher magnification of the [illegible] adenoma (X400)

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GROSS PATHOI BRONCHOSCOPI(

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uncommon As the obstruction becomes more complete and drainage to the affected lung is impaired chronic infection develops distal to the tumor site and the clinical picture becomes that of chronic suppurative disease of the lung with productive cough, fever, and chest pain This was the most frequent symptom complex in one half of the patients in our series Although the bronchial adenoma may be present as a silent lesion in only 2 of the 35 patients was this the case The tumors in these patients were found as asymptomatic pulmonary nodules on chest roentgenograms

The diagnosis of bronchial adenoma is usually not difficult The long duration of symptoms suggestive of bronchial obstruction associated with hemoptysis or chronic localized suppurative disease of the lung may lead the clinician to suspect the presence of an adenoma The tumor may be seen by means of bronchoscopic examination in a high per cent of cases (80 per cent of our series) and a biopsy taken The hazards associated with bleeding following biopsy have already been mentioned The surgeon should also be aware of the difficulty in making an accurate diagnosis pathologically on a small biopsy specimen There is not only considerable difference between the microscopic appearance of different tumors but also in the appearance of different areas of the same tumor For this reason a pathologic diagnosis made on a biopsy specimen should be accepted by the surgeon only if it is consistent with the clinical history and findings Papanicolaou smears of bronchial washings are usually negative for tumor cells The adenomas are covered in most instances by intact mucosa so that tumor cells are not found in the bronchial washings



Fig 5 Chest roentgenograms of a 32 year old woman showing a typical rounded hilar shadow caused by an adenoma This patient was asymptomatic The tumor was discovered on a routine survey film Patient alive and well four years after a right middle lobectomy

ROENTGEN APPEARANCE

The adenoma may present one of two roentgenographic patterns It may be seen on roentgenograms of the chest as a rounded smooth mass usually at or near the hilum in a patient without symptoms (Fig 5) This was the appearance in 2 of the 35 cases in this series More commonly however one finds the roentgen appearance associated with obstruction of a bronchus to a lung lobe or segment with loss of volume or obstructive pneumonitis of the involved portion of lung depending on the degree and mechanics of the obstruction Bronchograms and stratograms may be of great value in demonstrating the nature and site of the bronchial obstruction (Fig 6) Out of 35 patients in our series 26 had demonstrable lesions by one or more roentgenographic techniques

TREATMENT

Proper treatment of the bronchial adenoma must be based on an accurate diagnosis as well as a thorough knowledge of the long natural course of the tumor its tendency to recur locally after inadequate removal and its malignant potentialities Surgical removal of the tumor is the accepted treatment of choice Endoscopic removal was advocated for many years by some but now has been abandoned except in certain special situations There are several objections to bronchoscopic removal as a method of treatment of bronchial adenomas It has been shown that the portion of the tumor available for removal by bronchoscopy constitutes only a small part of the tumor in most cases [6] thus explaining the high rate of local recurrence after endoscopic removal Serious and even fatal bleeding



Fig. 6a & b Bronchograms of a 16 year old white girl who had had a cough and wheezing respirations for eighteen months A preoperative bronchogram (A) showed an obstruction caused by an adenoma in the left upper lobe A left upper lobectomy with a plastic repair of the bronchus was performed Post-operative bronchogram (B) with the remaining lower lobe expanded to fill the left chest (See Fig 7 bottom sketch for diagram of the bronchoplastic repair)

following endoscopic removal is not infre quent In the majority of cases the symp toms caused by the adenoma are those due to chronic suppurative disease associated with the bronchial obstruction In many instances these symptoms can be alleviated only by removal of the chronically infected lung distal to the obstructing adenoma Endoscopic removal may still be indicated however in severely debilitated elderly indi luals who would not tolerate operation it such patients constitute a very small ercent of patients with adenomas Re eated checks for recurrence are necessary f the adenoma is removed by broncho scopy because local recurrence can occur and has been reported as long as ten years after endoscop c removal Because of the slow growth and tendency to metastasize late in its course a limited resection is often adequate for complete removal of these tumors Bronchoplastic procedures which accomplish the complete removal of the tumor and yet preserve all lung uninvolved by tumor or chronic infection have their greatest usefulness in the treatment of this tumor Five of the 35 patients in this series had such procedures with excellen results (Fig 7) In most of our case however lobectomy or pneumonectomy wa necessary Lobectomy was performed eleven cases bilobectomy in nine and pne monectomy in five cases

IRRADIATION THERAPY

Irradiation therapy may be of value in the cylindromatous adenomas when surgical re moval is not possible We have used ir radiation therapy in two cases of recurrent cylindromas of the bronchus and in one extensive cylindroma of the trachea with perhaps some beneficial results There is very little evidence from reports in the litera ture that irradiation therapy has any effect on the carcinoid adenoma

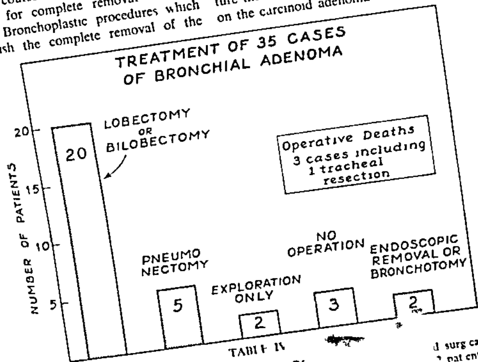


TABLE IV

Treatment of 35 cases of bronch al adenoma Of ... d surg cal exc on of the r tum r 21 ... pat ents are

ROENTGEN APPEARANCE

The adenoma may present one of two roentgenographic patterns It may be seen on roentgenograms of the chest as a rounded smooth mass usually at or near the hilum in a patient without symptoms (Fig 5) This was the appearance in 2 of the 35 cases in this series More commonly, however, one finds the roentgen appearance associated with obstruction of a bronchus to a lung, lobe, or segment with loss of volume or obstructive pneumonitis of the involved portion of lung depending on the degree and mechanics of the obstruction Bronchograms and stratograms may be of great value in demonstrating the nature and site of the bronchial obstruction (Fig 6) Out of 35 patients in our series 26 had demonstrable lesions by one or more roentgenographic techniques

TREATMENT

Proper treatment of the bronchial adenoma must be based on an accurate diagnosis as well as a thorough knowledge of the long natural course of the tumor, its tendency to recur locally after inadequate removal, and its malignant potentialities Surgical removal of the tumor is the accepted treatment of choice Endoscopic removal was advocated for many years by some but now has been abandoned except in certain special situations There are several objections to bronchoscopic removal as a method of treatment of bronchial adenomas It has been shown that the portion of the tumor available for removal by bronchoscopy constitutes only a small part of the tumor in most cases,[18] thus explaining the high rate of local recurrence after endoscopic removal Serious and even fatal bleeding

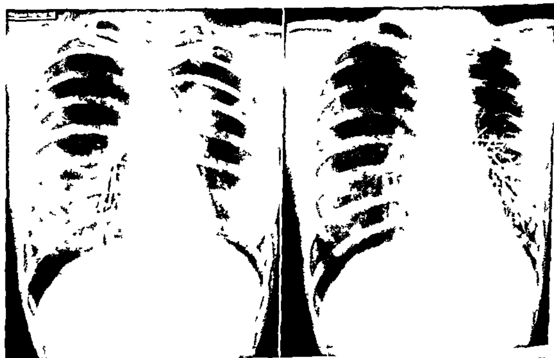


Fig 6a & b Bronchograms of a 16 year old white girl who had had a cough and wheezing respirations for eighteen months A preoperative bronchogram (A) showed an obstruction caused by an adenoma in the left upper lobe A left upper lobectomy with a plastic repair of the bronchus was performed Post operative bronchogram (B) with the remaining lower lobe expanded to fill the left chest (See Fig 7 bottom sketch for diagram of the bronchoplastic repair)

following endoscopic removal is not infrequent. In the majority of cases the symptoms caused by the adenoma are those due to chronic suppurative disease associated *with the bronchial obstruction.* In many instances these symptoms can be alleviated only by removal of the chronically infected lung distal to the obstructing adenoma. Endoscopic removal may still be indicated, however, in severely debilitated elderly individuals who would not tolerate operation but such patients constitute a very small percent of patients with adenomas. Repeated checks for recurrence are necessary if the adenoma is removed by bronchoscopy because local recurrence can occur and has been reported as long as ten years after endoscopic removal.[*] Because of the slow growth and tendency to metastasize late in its course a limited resection is often adequate for complete removal of these tumors. Bronchoplastic procedures which accomplish the complete removal of the tumor and yet preserve all lung uninvolved by tumor or chronic infection have their greatest usefulness in the treatment of this tumor. Five of the 35 patients in this series had such procedures with excellent results (Fig. 7). In most of our cases, however, lobectomy or pneumonectomy was necessary. Lobectomy was performed in eleven cases, bilobectomy in nine and pneumonectomy in five cases.

IRRADIATION THERAPY

Irradiation therapy may be of value in the cylindromatous adenomas when surgical removal is not possible.[22] We have used irradiation therapy in two cases of recurrent cylindromas of the bronchus and in one extensive cylindroma of the trachea with perhaps some beneficial results. There is very little evidence from reports in the literature that irradiation therapy has any effect on the carcinoid adenoma.

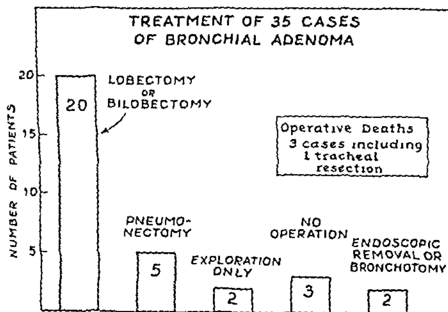


TABLE IX

Treatment of 35 cases of bronchial adenoma. Of the 25 patients who had surgical excision of their tumor 21 (84 per cent) are known to be living and well, 2 are dead and 2 have been lost to follow up.

RESULTS

The results of the surgical treatment of the adenomas and particularly of the carcinoid type have been very gratifying (Table IV) Out of a group of 20 patients who had either a lobectomy or bilobectomy 18 or 90 percent are known to be living and well as long as seventeen years after operation We have been unable to locate one patient and one died nineteen years after her original operation This patient had a left lower lobectomy for a cylindroma which recurred twelve years later in the bronchial stump A second operation was performed but resection was not possible because of the extensive spread of the tumor to pericardium, diaphragm, and mediastinum This patient lived for seven years after her second operation Five patients had a pneumonectomy performed and of this group three are living and well as long as seven years after operation One of the patients who had a pneumonectomy has been lost to follow up and another died eight years after her original operation This patient was a 39 year old woman who had a cylindroma of the left main bronchus removed by left pneumonectomy Seven years after operation she was found to have a cylindromatous adenoma in the right upper lobe which was removed by segmental resection This patient died several months after her second operation It is interesting that the only two late deaths in the resection cases have been in patients who had cylindromas

In three patients exploration only was done At the time of operation the tumor was found to be too extensive for resection One was in a 34 year old woman who had had repeated illnesses due to lung abscess and empyema requiring drainage on several occasions Pneumonectomy was attempted but was impossible because of extensive involvement of pericardium and pulmonary vessels The patient died a week later of complications of suppurative disease of the lung One of these patients died six years after exploration with metastases to the abdomen The other patient is still living three years after operation but with roentgen evidence of a large mediastinal mass

No operation was performed in three cases One patient refused operation after a bronchoscopic biopsy and is still living without symptoms sixteen years later Another patient who refused to accept surgical treatment died eight years later with metastases to the mediastinum and scalene nodes A third patient was not operated upon because of metastases to the spinal canal This patient was a 65 year old paraplegic with severe heart disease who for thirty years had had complete opacity of the left lung field on roentgen examination This was caused by obstruction of the bronchus by an adenoma which could be seen at the time of bronchoscopy

One patient in this series had a bronchoscopic removal of a small polypoid adenoma This patient is alive and free of evidence of recurrence seven years after removal Another patient had a very limited resection of an adenoma and a plastic repair of the defect without removal of any lung tissue (Fig 7) This patient is alive and free of recurrence eight years after operation

Bronchoplastic procedures have been performed in five patients (Fig 7) All of these cases have done well and have shown no evidence of recurrence in the period since operation which in one case has been as long as ten years Limited resection has been used wherever possible in order to preserve all lung tissue not involved by tumor or chronic infection " Goldman" has recommended consideration of local excision in every case where the following conditions can be met

The tumor

(1) is established to be benign, semi benign or only potentially malignant,

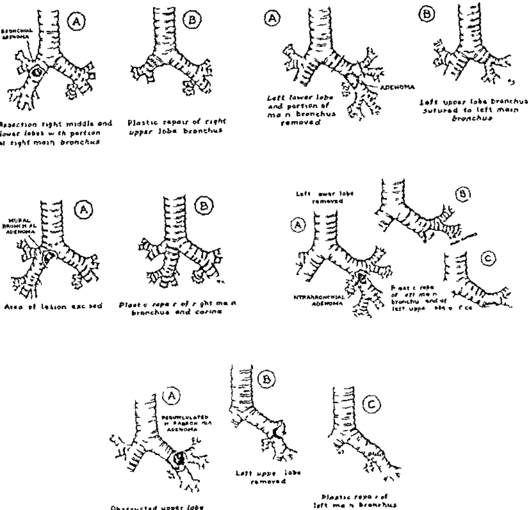


Fig 7 Bronchoplastic procedures done in 5 cases These patients are all alive and well from one to ten years following operation with no evidence of recurrence

(2) has not undergone malignant degeneration metastasized or widely infiltrated the bronchus,

(3) is located in the trachea or an easily accessible bronchus

(4) is localized has no extensive extrabronchial growth and has not caused pressure necrosis,

(5) has a stalklike or small area of sessile attachment,

(6) has caused no irreversible pulmonary damage in the lung distal to its location

Complete excision of the trachea was performed in one patient who had a cylindroma involving most of his thoracic trachea and extending downward to involve both the right and left main bronchi This patient was threatened with suffocation from complete tracheal obstruction Irradiation therapy had been tried but the obstruction became worse so this form of therapy was abandoned Approximately 12 cm of the trachea and bifurcation were resected and replaced with a prosthesis fashioned dermis over a coil of steel wire This p died two days following operatio

respiratory obstruction due to kinking of the major bronchi at the site of the anastomoses In two similar cases with one survival re ported by Belsey[18] resection of the entire tracheal circumference was not necessary Both of these cases had cylindromas re sected and the tracheal defect repaired with a prosthesis made of fascia from the patient s thigh and number 32 gauge stainless steel wire

OPERATIVE DEATHS AND COMPLICATIONS

There were 3 operative deaths One oc- curred following exploration mentioned above The second occurred in a 32 year old woman who expired on the operating table due to inadequate ventilation It was discovered too late that the endotracheal tube had slipped down into the right main bronchus The third death occurred follow- ing resection of the trachea for a cylin droma already referred to above

Postoperative complications occurred in 7 patients Two patients had postoperative hemorrhage necessitating re opening of the chest to control the bleeding One patient developed a superficial hematoma of the wound which caused a disruption requiring secondary closure Two patients developed an empyema following a small bronchial leak These cases were successfully treated by closed thoracotomy and tube drainage One patient had a collection of serosangui nous fluid in the chest requiring aspiration In one case there was roentgen evidence of infarction of the right lower lobe presumably due to damage to the blood supply at the time of operation This cleared without treatment

SUMMARY

The bronchial adenoma is a tumor which arises from the mucous glands and their ducts in the bronchial wall It is character istically a slow growing tumor which may be locally invasive or in a small percent of cases have distant metastases The clinical signs are those due either to the vascularity of the tumor with associated hemoptysis or to bronchial obstruction and chronic sup purative disease of the affected lung

The diagnosis is usually not difficult The long history of hemoptysis or localized suppurative disease of the lung associated with bronchial obstruction may lead the clinician to suspect the presence of an aden oma The tumor may be seen by means of bronchoscopic examination in the majority of patients Specialized roentgen technics such as stratograms or bronchograms may be of value in demonstrating the site and nature of a bronchial obstruction

Surgical excision of the adenoma is the treatment of choice Endoscopic removal is not recommended because of the likeli hood of recurrence the hazards of uncon trolled hemorrhage and the failure of this method of treatment to relieve the symptoms due to chronic suppurative disease in the lung distal to the adenoma The results in terms of complete removal of the tumor and relief of symptoms are excellent in patients in whom surgical excision is possible

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Conclusion

THE AUTHORS in presenting their philosophy *of treatment* evolved from a combined experience of 1215 patients having bronchial neoplasms hope to contribute to an improvement *in the results of both the* surgical and nonsurgical treatment of this disease They feel that this *improvement* can be made mainly by a better selection *of patients for surgical* excision and to a betterment in the quality of survival through application of selective resections of the lung in patients with suitable lesions It is realized that this attitude may represent a departure from the ideal of the traditional radical approach to the surgery of cancer *of an internal organ It is believed, however,* that the traditional concept must be tempered in the case of bronchogenic carcinoma by [illegible] and the [illegible] Churchi[illegible] cancer of the lung started with the very radical approach and swung back toward *a middle ground*, whereas the surgery of *every other organ started* with a limited and often inadequate resection and progressed toward a reasonable middle ground I think the answer to this is largely the stage of surgery at which resection for cancer of the lung began, and also simply from the technical fact that it is simpler and quicker to do a total pneumonectomy than it is to do a lobectomy with adequate *removal of the regional lymph nodes*" Regardless of philosophy of treatment even those who *advocate a radical resection for* bronchogenic carcinoma find themselves doing an increasing percentage of selective resections due to practical considerations of pulmonary function and cell type

The *classical temporal theory* of the *spread of a neoplasm and its prognosis* is now being challenged by an antithetic *theory designated as biologic predeterminism* The temporal theory emphasizes the function of time in the spread of cancer and states that a malignant neoplasm begins as a localized disease, grows in a steady and irrevocable manner, spreads to the regional lymph nodes in time and with the passage of *more time* disseminates throughout the body The classical temporal theory has *been generally accepted and forms the* logical basis for the traditional radical approach to carcinoma It implies that the majority of bronchogenic carcinomas can be diagnosed at a time when early and wide surgical eradication is possible provided patients and physicians alike are sufficiently aware of the early symptoms of the disease and present diagnostic techniques are fully utilized In this *concept, the existing methods of diag*nosis and treatment are considered adequate and responsib*ility for any delay in* detection during a localized phase is placed alike on the physician and the *individual concerned* This theory in its practical application puts a severe burden upon both the patient and the physician and leads to feelings of recrimination on the part of the patient and his family and contributes to a feeling of guilt upon the part of the physician when a diagnosis of bronchogenic carcinoma is made at a stage where surgical removal of

the lesion is impossible

The theory of biologic predeterminism is a tenable concept which explains the course and prognosis of cancer on the basis of the biologic characteristics involved The cell type the location, and the resistance of the host largely predetermine the pattern of behavior and prognosis, and the factor of time becomes less important as a consequence only of the biologic traits of the particular neoplasm involved The characteristics of an individual neoplasm are established in the preclinical phase and remain more or less constant throughout its life, although it may undergo intermittent periods of growth and quiescence (induced or spontaneous) Certain bronchial neoplasms, namely adeno, bronchiolar, and squamous cell carcinomas, may have a long natural history and may remain as localized tumors for even a period of years before extending beyond the site of origin Such lesions may be early biologically but late chronologically and ideal for surgical therapy Even within these cell types, however, certain neoplasms may be very orderly as far as their cell pattern is concerned but may be widely disseminated early with the production of only minimal symptoms because of an unfavorable location or lack of resistance on the part of the host The small cell un differentiated and to a lesser extent the large cell undifferentiated neoplasms as a group have a much shorter life history and usually cannot be diagnosed at a stage when they are amenable to surgical therapy except for those located peripherally Biologic predeterminism recognizes that the rate of growth of a neoplasm is an inherent characteristic depending on the biologic traits of the particular neoplasm involved, which may vary within the life history of the individual lesion and is affected by factors of cell type location and the resistance of the host tissues to its implantation and growth

Application of the theory of biologic predeterminism to bronchogenic carcinoma explains the variegated pattern of behavior and prognosis in this neoplasm and places the rationale of treatment on a logical basis It explains why approximately two out of three patients are not suitable for surgical therapy It dispels attitudes of therapeutic nihilism by fitting the treatment to the particular characteristics of the neoplasm involved It does not absolve the physician and the surgeon of the responsibility for diagnosis of the localized bronchogenic carcinomas that are suitable for resection and emphasizes the necessity of differentiating from this group the neoplasms which by their very nature are more suitable for other methods of therapy Nonsurgical therapeutic measures such as irradiation and chemotherapy, in this rationale of treatment, are not regarded as modalities to be used for surgical failures alone but rather for specific indications in that group of neoplasms for which surgery either is not indicated or is contraindicated Other forms of therapy are considered preferable to surgery under these circumstances

The selection of patients for surgery based on this rationale of treatment constitutes the most important single factor in the improvement of results of surgical therapy The fact that certain bronchial neoplasms may be detected while still in an early phase and thus are suitable for resection does not imply that all patients having bronchogenic carcinoma should be subjected to thoracotomy because it is the "only chance of cure" Neoplasms that have reached the general lymphatics or have become generalized as evidenced by distant blood stream metastases are no more amenable to surgical therapy than Hodgkin's disease or leukemia This attitude does not preclude frankly palliative resections for relief of specific distressing symptoms in an attempt to improve the quality of survival It does, however, deny the value to the patient of exploratory thoracotomy in stances where nonresectability is

and of meddlesome resections of lungs leaving behind gross neoplasm thus exposing the patient to rapid progression of the disease by breaking down natural barriers of resistance In the overall evaluation of results the harm that may have been done by ill advised surgery must be added to the negative column This harm is evidenced by the surgical mortality of exploratory thoracotomy for nonresectable lesions and the postoperative morbidity and shortening of survival time in this group of patients The fact that one half of patients die within the first year following resection emphasizes the difficulty of properly selecting patients for surgical therapy It is unrealistic to suggest that surgery has been of benefit to patients that survive for so short a period Paradoxical as it may seem reduction by careful screening of the number of patients deemed operable represents the best opportunity to improve the results of surgical treatment for bronchogenic carcinoma The surgeon before advising surgery must carefully consider the nature and the degree of localization of the neoplasm whether or not the patient can tolerate the proposed resection and live comfortably following it and be aware of other modalities of treatment that may be more suitably applied either alone or in combination in an attempt to control the neoplasm Only in this manner can the surgeon arrive at a rational solution to the problem of the patient having a malignant bronchial neoplasm

Based on this rationale of treatment it is believed that selective resection is the operation of choice in the surgical treatment of a patient having a bronchogenic carcinoma This should include removal of the hilar and mediastinal lymph nodes Experience has shown that a selective resection will be feasible in approximately one half of patients having bronchogenic carcinoma suitable for surgical therapy The majority of these patients having selective resection will have peripheral neoplasms some of which will have invaded the chest wall necessitating an en bloc resection of a portion of the chest wall Total pneumonectomy is indicated for peripheral neoplasms which have metastasized to hilar and mediastinal nodes unless considerations of pulmonary function make a lesser resection mandatory Pneumonectomy is more often indicated because of the site of origin of many epidermoid carcinomas in the lobar and main bronchi The necessity of making the bronchial section at least 1 5 cm from the point of visible neoplasm indicates total pneumonectomy for these tumors unless lobes can be preserved by bronchoplastic procedures Conservation of pulmonary tissue becomes increasingly important in patients in the age groups susceptible to primary neoplasms of the lung In the interest of the quality of survival surgical therapy must be applied so that patients may obtain maximum benefit without introduction of irreversible factors that may make it impossible for them to live comfortable and productive lives

Irradiation therapy which is capable of modifying the natural history of the neoplasm may bring about relief of distressing symptoms in many patients and occasionally results in an apparent cure The most frequent application of irradiation therapy will be for the neoplasm not suitable for surgical therapy because of extension into structures that cannot be safely resected or into the lymphatic system to an extent that precludes a successful resection Recurrent neoplasm following resection may often be held under control by irradiation therapy for several months giving gratifying relief of symptoms Irradiation therapy is useful in the control of pain due to cerebral and bony metastases Used preoperatively over hilar lesions that have infiltrated the bronchus close to the coryna and over neoplasms that have invaded the chest wall irradiation therapy

may cause a regression that will allow successful resection resulting in some cases in an apparent cure Bronchiolar and adenocarcinomas respond poorly to irradiation therapy The small cell undifferentiated carcinoma responds quickly to irradiation therapy but because of the tendency of this neoplasm to be widely disseminated the patient rarely survives for a long period of time Low grade epidermoid carcinomas fall midway in the scale of responsiveness to irradiation therapy but because of their tendency to be more localized may represent the best indications for irradiation therapy Irradiation therapy, like surgical therapy, suffers from the disadvantage of not being able to deal with disseminated disease Its use, however, in selected patients may be of great benefit in the overall management of patients having carcinoma of the lung

Chemotherapy, using the nitrogen mustard compounds, is the only presently available therapy of a specific nature that can modify the course of disseminated neoplasm All patients with a malignant bronchial neoplasm are potentially candidates for chemotherapy At the present time it is used alone in repeated courses in the treatment of patients having widely disseminated neoplasms It may be combined usefully with irradiation therapy using the latter modality over the primary neoplasm in the hope that chemotherapy will induce a remission of the growth of the more distant metastases Chemotherapy used in conjunction with surgical resection at the time of operation is not yet of proven value, but certainly deserves a thorough clinical trial since there is sound experimental evidence that it is capable of preventing to some degree the implantation of neoplastic cells that have invaded the blood stream The beneficial results of chemotherapy can more often be observed in the relief of distressing symptoms and in the production of a sense of well being rather than in a lengthening of survival time The ultimate hope of cancer research is that a substance will be found that taken internally will be cancerocidal or cancerostatic either by selectively destroying the cancer cell or by depriving it of some metabolic substance necessary for its survival

The terminal care of a patient having a bronchogenic carcinoma is the most important and yet the most easily neglected phase of the management of this disease The relief of suffering and the maintenance of morale is as much a responsibility of the physician as to cure Close cooperation between the specialist in the field of cancer therapy, the physician responsible for the intimate daily care of the patient, and the family can do much to relieve the distress of the terminal illness Every use should be made of all available measures to control unpleasant symptoms Above all the patient should never be allowed to gain the impression that he is being abandoned by the physician because nothing more in a curative sense can be done for him Some of the closest human relationships between a physician and his patient develop during the care of the incurable patient The patient and the family are eternally grateful for the attention and consideration shown by the physician during this trying period

The results of therapy in the treatment of bronchial neoplasms are subject to statistical analysis, insofar as numbers of survivors are concerned, but certain features such as quality of survival and length of survival time defy accurate analysis Patients may survive long periods of time before treatment is instituted or without any treatment A study of the authors' series along with those of other physicians treating this disease indicates that if a broad base of observation is maintained including histologically proven as well as those clinically diagnosed that approximately one

patients will be deemed suitable for surgical therapy One third of all patients will be found to be resectable although at the time of operation many of the resections may be considered palliative rather than curative Less than one fourth of patients having re sections of their bronchial neoplasms will survive five years Thus, the total salvage of the entire group in the terms of five year survival will be in the neighborhood of 7 per cent

There is danger in overgeneralization in quoting results of therapy Patients should be evaluated from the standpoint of prog nosis in relation to the group in which they fall at the time of recognition of the neo plasm Patients with small cell undifferenti ated carcinomas have little chance of surviving a year following diagnosis On the other hand patients with neoplasms presenting as peripheral pulmonary nodules without symptoms and without evidence of nodal metastases have a 70 per cent chance of surviving five years with a good quality of survival since most of these lesions can be removed by lobectomy It is difficult to show that irradiation and chemotherapy af fect survival time due to the lack of ade quate controls with similar untreated cases The observed ability of these modalities to improve the quality of survival however should not be overlooked The survival curves of patients having irradiation therapy as compared with those untreated are quite similar except that in the case of irradia tion therapy there will be a small percentage of patients alive at the end of five years who are apparently cured The great varia tion in the life history of neoplasms and the impossibility of determining the time of the origin of the neoplasm in a sense renders studies of survival time somewhat meaning

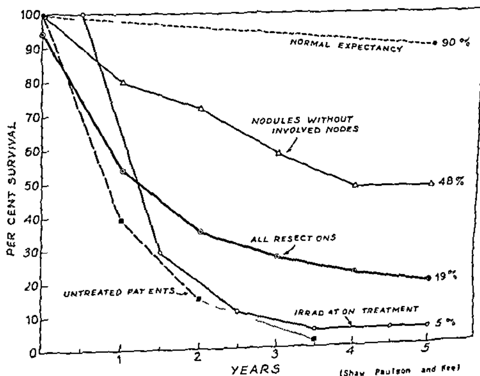


TABLE I

less The determination of onset of the disease by the first occurrence of symptoms is highly inaccurate due to the tendency of certain neoplasms to remain symptomless for several years and to the difficulty of determining that the symptom leading to investigation actually was caused by the neoplasm Presentation of survival curves should not suggest that the efficacy of the various methods of treatment are being compared (Table I) The patients comprising the groups both untreated and treated by various modalities are totally dissimilar and not subject to comparison Survival curves are useful, however, in giving a more accurate picture of the overall results of treatment of bronchial neoplasms and to allow a more realistic determination of prognosis in the individual patient by evaluating his outlook from the standpoint of the group within which he falls

The challenge today is to learn more about the biologic characteristics of the various types of bronchial neoplasms so that we will know which lesions are suitable for surgical resection and which are treated better by other means, which will be benefited by radical resections, and which may be treated by more conservative resections without sacrifice of survival time but with the attendant advantages of a lower mortality rate and a better quality of survival

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